MEDICAL PROCEEDINGS

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REDAKSIONEEL · EDITORIAL

DIE MEDIESE PRAKTYK BY DIE KRUISPAD

Die Mediese Diensplan is tans stewig gevestig in die proefgebied waarin dit van stapel gestuur is, en reëlings is reeds getref om die voordele daarvan tot beskikking te stel van deelnemende lede wat buite die primêre proefgebied in Suid-Transvaal werk, woon of besoek aflê.

In die praktyk beteken dit ook dat as 'n organisasie sy hoofkwartier aan die Rand het, sy werknemers in ander dele van die land deelnemende lede kan word. Hoewel dokters buite die proefgebied nog nie formeel as deelnemende dokters geregistreer is nie, sal hulle volgens die Plan as sodanig beskou word indien hulle bereid daartoe is.

By ons ter perse gaan het ons verneem dat die Plan reeds die steun geniet van 19 groepe met meer as 1,500 deelnemende lede en afhanklikes; en die onderhandelings wat op die oomblik met etlike groot organisasies gevoer word, dui op voortdurende belangstelling in en steeds toenemende steun vir die plan.

Ons lesers sal hulle herinner dat die Mediese Diensplan 'n nie-winssoekende onderlinge hulpvereniging is wat omvattende (in die praktyk feitlik algehele) dekking vir mediese, chirurgiese en hospitaalbehandeling aan die pasiënt verskaf. Die deelnemende dokter ontvang die gebruiklike private gelde vir persone met 'n gemiddelde inkomste.

Die finale tarief van gebruiklike private gelde is nog nie gepubliseer nie. Dit sal egter 'n tarief wees wat vasgestel word nie deur die

MEDICAL PRACTICE AT THE CROSS ROADS

The Medical Services Plan is now firmly established in the pilot area chosen for its launching and arrangements have already been made to extend the scope of its benefits to participating members who may work, live or visit outside the primary pilot area in the Southern Transvaal.

This also means, in effect, that where an organization has its headquarters in the Reef area, its employees in other parts of the country may now become participating members. Although doctors outside the pilot area have not yet been formally enrolled as participating doctors, the Plan will treat them as such if they are agreeable.

At the time of writing we understand that the Plan has already enrolled 19 groups with over 1,500 participating members and dependants; and the negotiations proceeding with several large organizations point to a continued interest in and progressive support for the Plan.

Our readers will recall that the Medical Services Plan is a non-profit Friendly Society which gives the patient comprehensive (in practice virtually total) cover for medical, surgical and hospital services. The participating doctor receives customary private fees for persons of average income.

The final tariff of customary private fees has not yet been published. It will, however, be a tariff determined not by the Plan or its participating doctors but by the Medical As-

Plan of deur die deelnemende dokters nie, maar deur die Mediese Vereniging van Suid-Afrika, en daarom sal dit waarborg dat die Plan nòg die publiek nòg die professie sal uitbuit.

Die Plan behoort 'n einde te maak aan die verderflike en ongeoorloofde stelsel in gevolg waarvan daar van die dokter verwag word om die diens wat hy self verskaf te subsidieer—'n toestand sonder weerga in die professionele, kommersiële of industriële sfeer.

Ons beklemtoon hierdie aspek van die Plan se betekenis vir die mediese professie omdat dit toevallig van stapel gestuur is juis op 'n tydstip toe kommersiële versekeringsmaatskappye begin het om vergoedingsdekking vir mediese versorging (nie diensvoordele nie) tot beskikking van die publiek te stel. In die geval van vergoedingsdekking vergoed die maatskappy die pasiënt geheel en al of gedeeltelik vir die uitgawes wat deur hom aangegaan is; in die geval van diensvoordele betaal die Fonds die dokter ten volle vir sy dienste.

Die professie moet op sy hoede wees vir die betalingsplan wat onlangs aangekondig is deur 'n sekere versekeringsmaatskappy wat in hierdie sfeer optree, naamlik The South African National Sickness and Accident Insurance Company (Sansom). Sonder om die mediese professie te raadpleeg, het hierdie Maatskappy besluit om 'n tjek, betaalbaar aan die dokter, uit te skryf. *Die bedrag word egter gebaseer op die verminderde tarief wat op Mediese Hulpverenigings van toepassing is,* soos goedgekeur en erken vir daardie doel deur die Mediese Vereniging van Suid-Afrika. Hierdie tjek word dan aan die pasiënt gestuur met 'n verklaring wat daarop neerkom dat dit redelik is dat die rekening teen die verminderde bedrag vereffen word, en waarin die polishouer uitgenooi word om dit as sodanig aan die geneesheer te bied.

Toestemming met so 'n reëling moet afgekeur word. Dit is 'n stelsel wat bes moontlik daarop kan uitloop dat 'n dokter 'n kleiner bedrag aanneem ter volle vereffening van sy rekening.

Dit is nodig om klem te lê op die feit dat daar hoegenaamd geen verband is tussen die spesiaal verminderde tarief wat op Mediese Hulpverenigings van toepassing is en die werksaamhede van 'n kommersiële versekeringsmaatskappy nie. Die tarief is opgestel as 'n kontrak tussen die georganiseerde professie en sekere nie-winssoekende onderlinge hulpverenigings, die merendeel van wie se lede binne 'n inkomstegroep ressorteer wat simpatiek deur die professie bejeën word. Dit was nie die bedoeling dat die tarief waaroor daar ooreengekom is, op enige manier verband moet hou met die skaal van private gelde nie. Dit was 'n voorreg wat toegestaan is aan verdienstelike groepe wat vir hierdie doel aan-

sociation of South Africa. This builds into the operation of the Plan a safeguard against exploitation for the public as well as the profession.

The Plan should spell an end to the pernicious and unwarranted practice whereby the doctor is expected to subsidize the service he provides—a situation without parallel in professional, commercial or industrial spheres.

We stress this aspect of the Plan's significance for the profession because it was launched most providentially at a time when commercial insurance companies had entered the field of providing indemnity cover (not service benefits) for medical care. In indemnity cover the company re-imburses the patient in whole or in part for the expenses incurred; in service benefits the Fund pays the doctor in full for his services.

The profession must be on guard against a manner of payment adopted by a particular insurance company operating in this field, viz. the South African National Sickness and Accident Insurance Company Limited (Sansom). This Company has decided (without consulting the medical profession) to make out a cheque payable to the doctor. *The amount is based on the reduced fee applicable to Medical Aid Societies* approved and recognized for the purpose by the Medical Association of South Africa. This cheque is forwarded to the patient with a statement which means in effect that it is reasonable that the account should be settled at the reduced fee, and the policy holder is invited to tender it as such to the doctor.

Acquiescence in such an arrangement is to be condemned. It is a procedure which may well have the effect of causing a doctor to accept a reduced fee in full settlement of his account.

It is necesary to stress the fact that the specially reduced tariff for Medical Aid Societies has no relevance to the operation of commercial insurance companies. The tariff was devised as a contract between the organized profession and certain non-profit Friendly Societies, most of whose members fall within an income group deserving the sympathetic consideration of the profession. The tariff agreed upon was not intended to be related in any way to scales of private fees. It was a privilege accorded deserving groups who have to apply for this purpose for approval (by the organized profession) of their constitution and composition.

We regard it as entirely deplorable that a commercial insurance company should uni-

soek om goedkeuring van hul konstitusie en samestelling deur die georganiseerde professie moet doen.

Ons beskou dit as volkome betreurenswaardig dat 'n kommersiële versekeringsmaatskappy sommer op eie houtjie en sonder die verlof van die Mediese Vereniging op hierdie verminderde tarief van doktersgelde (wat vir 'n heeltemal ander en trouens 'n liefdadigheidsdoel opgestel is) wil staat maak en dit wil gebruik as basis vir die betaling aan die praktisyn van 'n kleiner bedrag as dié wat aan hom toekom.

In hierdie gevalle meld die polishouer hom aanvanklik as 'n private pasiënt aan; maar die dokter word later 'n tjek aangebied vir 'n bedrag gebaseer op 'n verminderde tarief wat nie in hierdie omstandighede van toepassing is nie.

Ons beklemtoon die noodsaaklikheid daarvan om te voorkom dat ons kollegas in 'n uiters onbenydenswaardige posisie geplaas word vir sover dit hul pasiënte betref.

Die professie behoort hom te verset teen voorskrifte deur 'n buite-organisasie (in hierdie geval 'n kommersiële versekeringsmaatskappy) oor die wyse waarop hy sy eie sake moet reël, en ons wil by ons kollegas daarop aandring om te volhard in 'n waardige weiering om betalings wat op hierdie manier gedoen word, aan te neem.

Ons waarsku ons kollegas om hierdie soort optrede nie goed te keur nie, want dit kan pasiënte bes moontlik aanmoedig om ter wille van verminderde doktersgelde van getrouheid te verander —'n ernstige en nie onwaarskynlike gevolg van toestemming met Sansom se vorstelle aan hul polishouers.

Ons wys op die ekonomiese gevare van hierdie beleid wat die ekonomiese hoekstene van die mediese professie kan ondermyn en aldus ons professionele maatstawwe in gevaar kan stel.

Die saak eindig egter nie hier nie. Sansom het verder gegaan en sy beleid kan bes moontlik 'n besonder ernstige dilemma vir die professie meebring. In 'n onlangse omsendbrief verklaar die maatskappy:

'Sommige firmas verkies dat alle eise deur hul werknemers by hul eie kantore ingelewer moet word sodat die firma self hierdie eisvorms ongeveer eenmaal per week aan Sansom kan voorlê. Dan is dit moontlik vir die Personeelafdeling van die betrokke firma om kennis op te doen van die gesondheidstoestand van hul personeel wat dikwels 'n uitwerking op die werk van die lid het.'

Goedkeuring van so 'n voorstel kom neer op die vernietiging van die professionele geheimhouding wat so 'n onontbeerlike vereiste vir 'n bevredigende verhouding tussen dokter en pasiënt is. Ons praktiseer nie in die geneeskunde vir die gerief van boekhouers of om dit makliker te maak om die neus in die private sake van ons pasiënte te steek nie. Almal wat waarde heg aan die standaarde van etiese gedrag waarby die mediese professie hom met Hippokratiese toegewydheid neerlê, sal verontrus wees oor die rampspoedige moontlikhede van hierdie beleid, en sal met kragdaadigheid daarteen te velde trek.

As daar ooit 'n tyd vir die hele mediese professie was om skouer aan skouer te staan om sy eie sowel as die publiek se belange te verdedig, en om sy lotgevalle in sy eie hande te hou, dan is dit in hierdie stryd wat nou klaarblyklik tussen die mediese professie en diegene wat daarbuite staan, ontbrand. Ons moet voorkom dat 'n posisie geskep word waar die professie in so 'n mate gekniehalter word dat hy net tot onderwerping, en niks anders nie, in staat is.

laterally and without any authority from the Medical Association seize upon a reduced tariff of fees (devised for an entirely different, indeed charitable, purpose) as the basis for paying the practitioner less than is his due.

In this case the policy holder presents himself in the first place ostensibly and in good faith as a private patient; but the doctor is subsequently tendered a cheque based on a reduced tariff not applicable in these circumstances. We emphasize the need to protect our colleagues from being placed in a most invidious position in relation to their patients.

The profession should reject dictation by an outside agency (in this case a commercial insurance company) of the manner in which it shall conduct its affairs and we urge our colleagues to persist in a dignified refusal to accept payments made in this way.

We warn our colleagues against countenancing any action of this kind, as it may well have the effect of encouraging patients to change their allegiance for cut-rate fees—a serious and not unlikely consequence of acquiescence in Sansom's proposal to their policy holders.

We point to the economic dangers of this policy, which may undermine the economic foundations of medical practice and so imperil its professional standards.

The matter, however, does not end here. Sansom has gone further and its policy may involve the profession in a most serious ethical dilemma. It states in a recent circular:

'Some firms prefer that all claims intimated by their employees should be handed in at their own offices so that the firm itself can submit these claim forms approximately once a week to Sansom. It is then possible for the Personnel Department of the firm to acquaint itself with the health conditions of their staff which often have an effect on the work of the member.'

To accede to such a proposition is to destroy the professional secrecy which is an essential ingredient in a satisfactory doctor-patient relationship. We do not practise medicine for the convenience of book-keepers or to facilitate probing into the private lives of our patients. All who value the standards of ethical conduct to which the medical profession subscribes with Hippocratic devotion will be dismayed by the potentialities for disaster revealed by these policies and will firmly oppose them.

If ever there was a time for the whole medical profession to stand united in defence of its own as well as the public interest, and to ensure the retention of the control of its own destiny in its own hands, it is now in this struggle which is developing between the medical profession and those outside it. We must prevent a situation whereby the profession is knee-haltered and rendered incapable of anything except of acts of submission.

PENICILLIN 152

A NEW ORAL SYNTHETIC PENICILLIN

An important report in the field of penicillin research was released at the annual Symposium on Antibiotics held in Washington at the beginning of this month.

This advance in penicillin therapy is based on the fact that the nucleus of the penicillin molecule (6-aminopenicillanic acid) has been isolated. In March 1957 Sheehan, of the Massachusetts Institute of Technology, in co-operation with research workers at Bristol Laboratories in the U.S.A., effected the total synthesis of the penicillin molecule. To-day the nucleus of the molecule (as the result of a process developed by the Beecham Research Laboratories in England) can be produced in large quantities by fermentation.

6-Aminopenicillanic acid has very poor antibacterial properties; but its isolation makes it possible for the organic chemist to tack any number of side chains on to the heart of the penicillin molecule. In this way Bristol scientists have been able to prepare over one thousand new variants of penicillin. These have been brought down to a short list of 60 products meriting further investigation and from this number one particular derivative (penicillin 152) has passed the stringent requirements for release as an addition to the antibiotic armamentarium.

Penicillin 152 is important because it represents an entirely new approach to the problem creating potent (and possibly safer) penicillins. Novel properties may now be grafted on to the penicillin nucleus and so provide a combination of effects inconceivable on the basis of a product derived from the unaided efforts of the mould itself.

Several striking claims have been made for penicillin 152:

It is extremely active when given by mouth. Its greater absorbability leads very rapidly to higher blood levels than have been attained before by other oral penicillins. These higher blood levels may be of great value with micro-organisms of only moderate penicillin sensitivity, where doubling the blood concentration may be essential for effective bactericidal action. In addition, these higher blood levels may be necessary where there is infection in areas with a poor blood supply.

Levels obtained within the first hour after oral administration of penicillin 152 give a concentration roughly twice as high as that following penicillin V administered in similar circumstances. The blood levels attained are also much higher than those with intramuscular procaine penicillin G.

Penicillin 152 is excreted very rapidly and it appears in ascitic and pleural fluids after oral administration.

The *in vitro* antibacterial spectrum of penicillin 152 is roughly equivalent to that of potassium penicillin V. Both drugs are highly effective against penicillin-susceptible staphylococci and against pneumococci, streptococci, gonococci and Corynebacteria. Penicillin 152 will therefore undoubtedly have a place in the treatment of bacterial infections due to the usual penicillin-sensitive organisms.*

As with other forms of penicillin, penicillin 152 is not recommended in deep-seated or chronic infections.

The *in vivo* spectrum of this new penicillin is reflected in the reports of 13 investigators, who have carried out clinical studies on over 500 patients. Streptococcal, gonococcal, staphylococcal and pneumococcal infections have responded rapidly to therapy with penicillin 152, which has also been tested against a large number of strains of *Staph. aureus* isolated from clinical sources. Many organisms resistant to penicillin G and penicillin V proved sensitive to penicillin 152.

In one investigation sensitivity tests were performed on 39 resistant strains of *Staph. aureus*. All were resistant or moderately resistant to penicillin G. Only 3 were sensitive to penicillin V. However, 16 (43% of these strains) proved sensitive to penicillin 152. In 34 of 39 cases, penicillin 152 produced effective inhibition at a concentration lower than that required for either of the other antibiotics.

There is evidence that penicillin 152 is more active than the older penicillins against resistant strains of staphylococci, both in the test tube and in challenging experimentally induced infections in laboratory animals. This fact is probably related to its slower destruction by penicillinase, the enzyme produced by resistant organisms, particularly the resistant staphylococci.

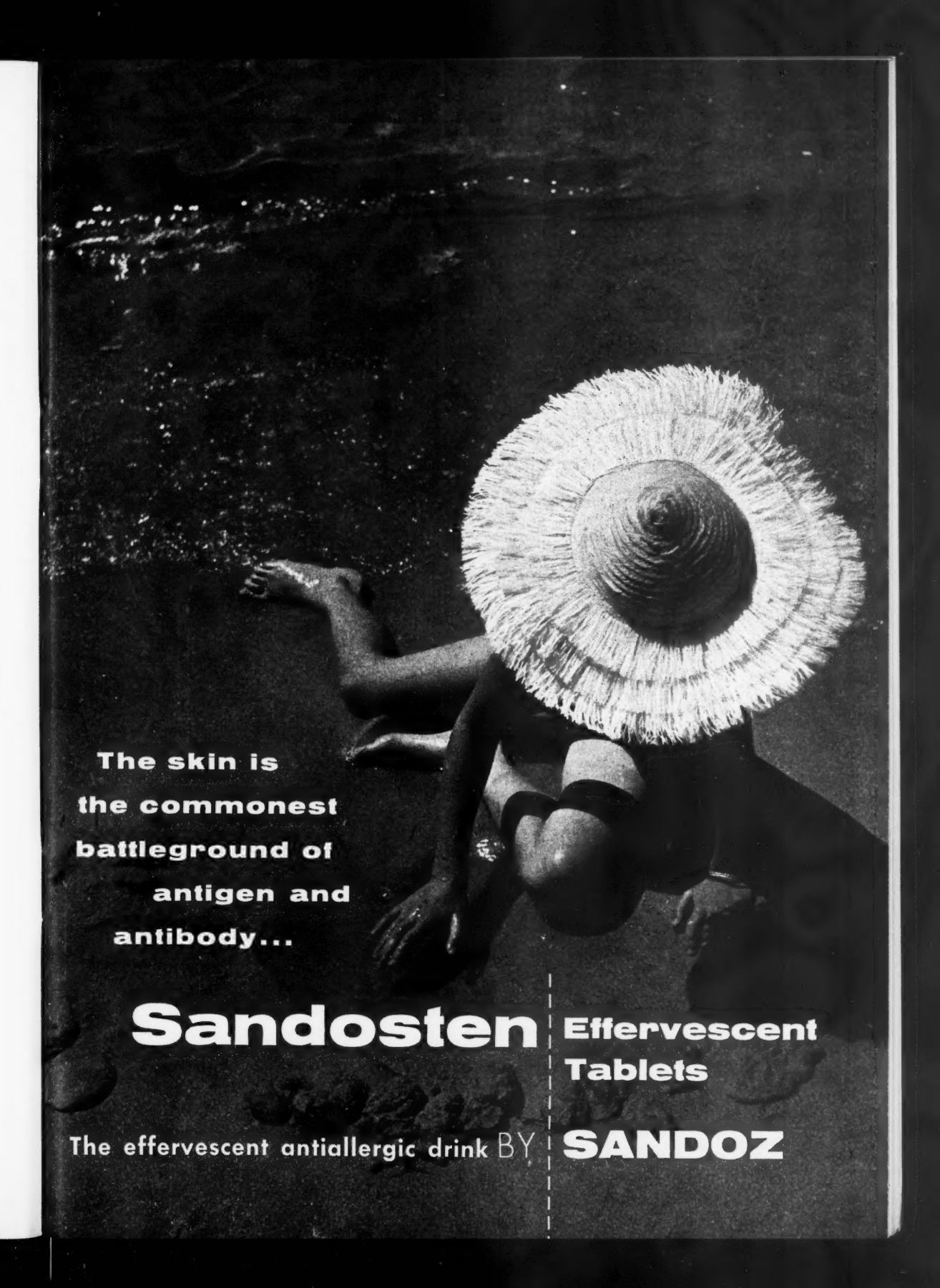
This new attack on the penicillin molecule may make possible the production of a modi-

*Respiratory tract infections, acute pharyngitis, septic sore throat, tonsillitis, otitis media, laryngitis, cervical adenitis, bronchitis and lobar or bronchopneumonia.

Skin, soft tissue and surgical infections, erysipelas, cellulitis, lymphangitis, wound infections and pyoderma.

Urinary tract infections, gonorrhoea, acute and chronic cystitis, pyelonephritis and prostatitis.

Scarlet fever, puerperal sepsis.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fication which does not share with the naturally occurring substance the allergenicity which has become so striking a feature of penicillin therapy.

In one report on 9 patients with histories of previous allergic reactions to penicillin, there is evidence that one of the patients developed itching (without a rash) during penicillin 152 treatment. The drug was discontinued and the itching responded to anti-histamine therapy. The other 8 patients with a history of penicillin sensitivity did not develop any allergic reaction to penicillin 152. These facts are clearly insufficient to justify definite conclusions about the comparative allergenicity of the new penicillin *vis-à-vis* other penicillins. It is, however, an aspect which will be watched with considerable attention.

The new interest created in the penicillin family is unlikely to end with the development of penicillin 152, the offspring of the side-chains which have been tacked on to the nucleus. The nucleus itself is a citadel which can expect to be assaulted. Already in cephalosporin C we have an antibiotic related to the penicillin family and which is insensitive to penicillinase. But the unusual properties in this case are due to a modification in the nucleus, not in the side chain.

The latest synthetic attack on the problem of creating safe and potent penicillins, as effective by mouth as by injection, opens up fascinating possibilities and has infinitely extended the antibiotic horizon. We can expect further remarkable developments on this front in the near future.

THE TREATMENT OF CORONARY ARTERY DISEASE WITH PARENTERAL MAGNESIUM SULPHATE

Elsewhere in this issue we publish a paper from Tasmania on the treatment of coronary artery disease with parenteral magnesium sulphate. The Tasmanian workers provide interesting confirmation of observations first made in this field by Malkiel-Shapiro, Bersohn and Terner.[1] Indeed, the Tasmanian results indicate an even more striking effect than was originally reported by the local investigators.

The South African observers not only indicated the possible clinical value of magnesium sulphate in the management of coronary artery disease, but they also recorded certain biochemical effects produced by this treatment.

It is interesting to note that Perlia[2] has also reported the definite clinical value of parenteral magnesium sulphate in the treatment of angina pectoris and coronary thrombosis.

Agranat,[3] in a careful evaluation of 50 cases of angina pectoris treated in this way, concluded that the use of magnesium sulphate in angina pectoris, on the information available at present, appeared to be worthwhile.

Sandler and McGregor,[4] on the basis of a study of 16 cases and using different criteria in the selection of their clinical material from those adopted by Malkiel-Shapiro, Bersohn and Terner, concluded that the improvement observed on parenteral magnesium sulphate was no greater than that attained with a placebo. Malkiel-Shapiro and Bersohn,[5] have analysed this claim very fully and critically.

Bersohn[6] has presented a possible explanation of the effects observed and suggested that in magnesium metabolism we may well find the link between the atherogenic and the thrombogenic components involved in intravascular clotting.

Recently Anstall *et al.*[7] reported that magnesium, even when given by mouth, tended to prolong the coagulation of the blood, i.e. magnesium has a definitely beneficial effect, from the patient's point of view, on the clotting mechanism of whole blood. In our present issue, Parsons, Butler and Sellars, in addition to confirming the biochemical changes described in the lipid pattern, now also show that magnesium enhances the fibrinolytic activity of the blood. This observation links the thrombogenic and the atherogenic mechanisms referred to.

It must be stressed that no adequately controlled clinical studies have yet been carried out so far on this therapeutic claim. The Tasmanian data, however, provide the nearest approach as yet to an extensive survey in that observations were made in the same hospital in 2 successive years. In the first year the mortality rate in cases of coronary artery disease treated by anti-coagulants was 30%. In the following year, with the addition of parenteral magnesium sulphate, the mortality rate was 1%. This, incidentally, supports the original South African claims made on the clinical effects.

Although the clinical case is not yet definitely proved, there seems to be a growing mass of evidence, in experimental animals as well as in Man, to indicate that magnesium sulphate may well have an important therapeutic action in this field.

It is certainly desirable that clinical trials on a large scale and under properly controlled conditions should be extended to test this interesting hypothesis.

1. Malkiel-Shapiro, B., Bersohn, I. and Terner, P. (1956): Med. Proc., **2**, 455.
2. Perlia, A. H. (1956): Sovetsk. Med., **20**, 63.
3. Agranat, A. L. (1958): Med. Proc., **4**, 67.
4. Sandler, A. and McGregor, M. (1958): S. Afr. Med. J., **32**, 697.
5. Malkiel-Shapiro, B. and Bersohn, I. (1958): S. Afr. Med. J., **32**, 1031.
6. Bersohn, I. (1958): Med. Proc., **4**, 62.
7. Anstall, H. B., Huntsman, R. G., Weitzman, D., Lehman, H. and Hayward, G. H. (1959): Lancet **1**, 814.

BREAST CONDITIONS

WHICH REQUIRE CLARIFICATION

3. BLEEDING FROM THE NIPPLE

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Johannesburg

(*Continued from p.* 89)

Discharge from the nipple is not uncommon and in most cases it is bloody. It causes distress to patients and there is no unanimity amongst doctors in regard to management. Simple mastectomy is often done for bleeding from the nipple. Is this good treatment or needless mutilation?

Purpose. This paper sets out to review the literature and to analyse my own experience with bleeding nipples. A group of cases from my records will be reviewed and the lessons learnt set out.

Discharge from the nipple is physiological during the reproductive and lactation period. At other times it is pathological. Beasley,[1] however, states that discharge can be expressed from 92% of apparently normal breasts.

MATERIAL REVIEWED

I have reviewed 805 cases of breast pathology seen in private practice over a period from 25 May 1934 to the end of 1957. Thirty-five cases were excluded because of insufficient data, leaving a total of 770. The significance of discharge from the nipple was one of the objects of the investigation.

There were 78 cases with nipple discharge, a percentage of 10.1.

Nature of the Discharge. Bloody or brown discharges are important. Other types are of little significance as the clinical condition of the breast determines treatment.

Cancer. There were 263 cases of cancer of the breast. In 87 of these no operation was done. In many the condition was too advanced for surgery. Others were referred to hospital for treatment. The cases were all florid ones where the diagnosis seemed beyond doubt. In none of this group of 87 cases was there at any time nipple discharge. There were 178 operated cases of breast cancer in which histological proof of the disease was forthcoming. In 5 of these a nipple discharge had existed. In 3 it was bloody though sometimes purulent. In one it was serous. In the remaining case the doctor had expressed putty-like material 9 months before. Thus in 263 cases of cancer of the breast a discharge had existed in 5 (1.9%).

Benign Breast Conditions. Five hundred and seven cases were reviewed. Nipple discharge existed in 73 cases, i.e. 14.4%. Of these 71% were bloody. Thus 10% of these 507 had blood-stained discharge from the nipple. Thirty-five of these cases were not operated on; in 14 of the latter the discharge was bloody, in 2 black, and the remainder showed serous, milky or purulent discharge. In 20 of these 35 cases there was no associated pathology detected. The other 15 had nodular breasts. Operation was not done in these cases either because there was no indication for it or because the patients were averse to surgery.

Operation was carried out in 38 cases of bleeding from the nipple. In 12 of these cases there was associated pathology, usually the nodularity of fibro-adenosis, mastitic plaques or thickening. At operation on these 12 cases, intraduct papilloma was found in 8. In 2 no papillomata were detected and the bleeding was attributed to papillary changes in the ducts. In the remaining 2 cases no papilloma was found but in the tissue removed spheroidal cell carcinoma was demonstrated.

In the 26 cases where nipple bleeding was the only evidence of breast pathology, operation disclosed the following:

In 21 duct papillomata were found. In 2 of these there was malignant degeneration of a papilloma one of which showed blood in many ducts.

In one case there was no papilloma, but a comedo carcinoma was found, with blood in many ducts.

In 4 cases no duct papilloma was found, but papillary duct changes of fibro-adenosis existed; in 2 of these cases fluid was expressible from several ducts of one nipple, serous from one duct, blood from another. This association suggests fibro-adenosis.

Thus in 26 cases where bleeding from the nipple was the only clinical evidence of breast pathology, cancer was found in three.

* Consulting Surgeon, Johannesburg General Hospital; Honorary Research Associate, Department of Surgery, University of the Witwatersrand.

DISCUSSION

THE SIGNIFICANCE OF NIPPLE DISCHARGE IN BREAST CANCER

In this series of 263 cases of cancer of the breast, nipple discharge varying from serous to bloody was found in 5, i.e. 1.9%. Aird[2] states that patients with cancer of the breast almost never give the history of any previous discharge. He has seen only one such case and then the bleeding was from the opposite unaffected side.

Treves[3] reported that in 1,000 cases of carcinoma of the breast, bleeding from the nipple was the original symptom in 2%. Treves and Holleb[4] reported 549 cases of cancer of the breast in women of 35 years or younger. Nipple discharge was present in 18, i.e. 5.5%, and there were more cases of bloody than of serous discharge. Bloody discharge more often indicated an infiltrating duct carcinoma with no papillary component. The average age of operated cases of cancer of the breast in the present series was 50.2 years, the youngest being 24 and the oldest 79.

Haagensen, Stout and Phillips,[5] from the Presbyterian Hospital in the City of New York, found that 1.3% of carcinomas of the breast were associated with serous or bloody discharge from the nipple.

CONCLUSION

Discharge from the nipple is rare as a symptom of cancer of the breast and is overshadowed in importance by the clinical evidence of the disease.

NIPPLE DISCHARGE IN APPARENTLY BENIGN BREAST CONDITIONS

These cases fall into two groups:

(*a*) Those with other evidence of breast pathology; and

(*b*) Those in which the discharge is the only evidence of breast disease.

In 507 cases of clinically benign breast lesions in this series, nipple discharge occurred in 73 cases, i.e. 14.4%. It was bloody in 52 cases.

In this group of 73 cases with discharge there were 27 with other clinical evidence of breast pathology. This took the form of some manifestation of fibro-adenosis. Twelve of these were operated on because of bleeding from the nipple. Intraduct papilloma was found in 8, and in 2 the bleeding was attributed to fibro-adenosis. In 2 cases unsuspected spheroidal cell carcinoma was found.

Thus the presence of a bloody discharge from the nipple led to the detection of 2 cases of occult cancer in a group of 12 operated on for bleeding from the nipple in supposedly simple conditions—cases in which operation would not otherwise have been carried out.

CONCLUSION

Bleeding from the nipple in cases of plaques, thickenings or nodules in the breast is an indication for exploration.

IS A DISCHARGING NIPPLE SERIOUS?

Madalin, Clagett and McDonald,[6] of the Mayo Clinic, sectioned on a slicing machine 100 breasts from 85 patients. They were removed by simple mastectomy for discharge from the nipple. Breasts ablated as a palliative procedure for carcinoma were excluded. Forty-two of the breasts examined contained localized or diffuse masses. The discharge was recorded clinically as bloody in 50, serous in 32, and of different colours in 18. In only one case was malignancy found. There was no evidence of this clinically, but in their investigation they found a microscopic focus of comedo carcinoma. This woman aged 41 had had the other breast removed previously by radical mastectomy for adeno-carcinoma.

Handfield-Jones and Porritt[7] consider that the same importance attaches to serous as to bloody discharge though the latter does not in itself imply malignancy. Allen *et al.*[8] say that the most likely cause of a bloody discharge from the nipple is a benign intraduct papilloma but that carcinoma is an occasional cause. Wakeley[9] operated on 119 patients with bleeding from the nipple. He found malignancy in 37 (31%). No reference is, however, made to the clinical state of the breasts in these cases.

Cole and Rossiter[10] list the commonest causes of discharge from the nipple as duct papilloma, carcinoma and chronic mastitis, in that order of frequency. This is in accordance with the findings in the present survey. They quote Hinchey[11] who found that in 67 patients in whom there was a serous or bloody discharge cancer existed in 23 (35%). Donnelly[12] reports that nipple discharge occurred in 219 (9.6%) of 2,269 patients examined for breast lesions. In 115 (5.2%) the discharge was bloody and in 53% of these carcinoma was found. Fitts *et al.*[13] report their investigations in the Pathology Department in 1,000

specimens of breast lesions. Nipple discharge had occurred in 31% of cases with papillomas, 3% with mastitis, 7% with carcinoma and none with benign lesions. Fitz and Horn,[14] in discussing occult carcinoma of the breast, report 4 cases in which nipple discharge was the only indication of pathology in the breast and, on exploration, carcinoma was found. The nipple discharge was serous, milky or bloody. In cases where bleeding from the nipple is the only indication of breast pathology, Aird[2] advises that if blood can be expressed from a part of the breast, the affected duct should be explored, but if there is no means of localizing the site of the bleeding, then watch the case under 50 and, if over that age, perhaps a simple mastectomy should be done.

At the Postgraduate School at Hammersmith in London, over a period of 7 years of uniformly conservative management of cases of bleeding from the nipple in the absence of a mass, not a single case of cancer developed.

In this series of 26 cases of bleeding from the nipple in the absence of other breast pathology, carcinoma was found in 3 (11.5%).

COMMENT

Bleeding from the nipple in cases where there is no other clinical evidence of breast pathology does not imply carcinoma. There is however no room for complacency in the management of these cases, as many (though by no means all) authorities report associated occult carcinoma in an appreciable percentage of cases. I would liken the risk of carcinoma in such cases to that which obtains in adenoma of the thyroid—about 10%.

THE RELATIONSHIP OF DUCT PAPILLOMA TO CARCINOMA

Haagensen *et al.*[5] state that, in their experience at the Presbyterian Hospital in New York, they have no evidence that intraduct papilloma, even when persisting for many years, transforms into papillary carcinoma. They make the important point that in rare instances intraduct papilloma and carcinoma may occur independently in the same breast.

In two of the cases of occult cancer in this series, where nipple bleeding was the only clinical indication of breast pathology, the cancer was the result of malignant degeneration in a duct papilloma.

One of these cases deserves special mention:

Mrs. H., aged 53, para 3, was referred to me by Dr. Rose Baranov in 1946. Serum had leaked from the left nipple for 3 weeks. The discharge was now bloody. The breasts were otherwise healthy. On 18 October 1946 papillectomy was carried out. The histology was that of an intraduct papilloma. In 1949 a serous discharge came from the opposite (right) nipple. Four years ago, i.e. 8 years after the first papillectomy, bleeding occurred from the right nipple and a papilloma was removed by another surgeon.

On 24 November 1958 the patient, now aged 65 years old, was referred back to me by her doctor. She had recently become aware of a mass below and medial to the left nipple. This was ill defined but not hard. There were no glands present. The other breast was normal.

On 25 November 1958 the mass was widely removed. Prof. James Murray of the South African Institute for Medical Research examined the fresh specimen. A tumour, a centimetre or more across was found; it was soft and brown and frozen section was not definitive. Stained sections were reported on as follows:

Macroscopic examination of this specimen from the breast shows the presence of a well-circumscribed, fleshy, lobulated tumour mass 1.0 cm. in its greatest diameter.

Sections through the tumour at several levels show the presence of multiple intraduct papillomata including the large mass observed macrospically. The papillomata consist of rather thin vascular connective tissue cores covered by multiple layers of cuboidal epithelial cells. In some areas the stroma shows hyalinization. The epithelial cells show very little dedifferentiation or loss of polarity and mitotic figures are scanty. In the most cellular areas there tends to be a cribriform arrangement of the epithelium, but at all points the growth appears to be confined within the duct walls and is not infiltrating the adjacent supporting tissue. The presence of malignant change is confirmed however by the finding of one or two tumour emboli in vascular and lymphatic channels.

The histopathological features are those of an intraduct papilloma in which early low grade carcinomatous change has occurred.

A simple mastectomy was done on 28 November 1958. The histological report reads as follows:

Three blocks have been taken from the subareolar area of the remaining breast tissue. Multiple intraduct papillomata have been observed in a large number of the ducts but no evidence of malignant neoplasia has been observed in any of these sections. In one of the sections a small sharply defined focus of fibroepitheliosis was observed.

She was referred to Dr. M. Weinbren for deep X-ray therapy.

MANAGEMENT OF CASES OF BLEEDING FROM THE NIPPLE

In all cases where blood can be expressed from the nipple, exploration should be done.

The patient is informed that a small operation is necessary to find and remove the source of the bleeding. This is most likely (90%) to be a small wart, the removal of which, by a non-mutilating procedure, will cure the condition. There is, however, the possibility (10%) that the condition may be more serious, when it would entail removal of the breast.

The patient is asked not to squeeze the nipple to evacuate discharge because if the surgeon cannot express discharge in the theatre before anaesthesia, the operation is postponed until discharge can be demonstrated in the affected duct. The patient is moreover warned that (*a*) the surgeon may fail to find the papilloma and (*b*) that if he does remove it, there may be others which may require further search at a later date. This occurred only once in this series of cases.

The affected duct orifice should be probed, the duct slit open and search made for a duct papilloma (McGregor).[15] If one is not found, the incision is extended freely on to the breast itself and a generous wedge of tissue removed for histological study. Simple mastectomy is not indicated as the routine treatment of bleeding from the nipple.

NON-BLOODY DISCHARGE FROM THE NIPPLE

Serous, or other non-bloody discharges from the breast, have in my experience no significance apart from what is associated with the clinical condition of the breast. Such discharges are therefore no cause for concern or for operation. Brown discharges are grouped with bloody ones as Madalin *et al.*[6] found blood and duct papillomata in the ducts of such cases.

CONCLUSIONS

In 770 cases of breast disease nipple discharge occurred in 78 (10.1%).

Nipple discharge is rare in cases of cancer of the breast (1.9%).

Serous and other non-bloody discharges have no significance apart from that of the associated pathology.

Bloody discharge from the breast may be associated with other breast pathology or may be the only indication of abnormality. It is in relation to the management of the latter group that such wide differences of opinion exist.

In the 26 cases reported here duct papilloma was much the commonest cause. Occult carcinoma was found in 3 (11.5%). In two of these this was due to malignant degeneration in a duct papilloma.

The treatment of bleeding from the nipple is exploration of the duct from which blood is expressed, and such further action as is indicated by the findings.

Mastectomy as a primary procedure should not be done.

OPSOMMING

In 770 gevalle van borskwaal is 'n tepelafskeiding by 78 (10.1%) waargeneem.

Tepelafskeiding is 'n seldsame verskynsel in gevalle van borskanker (1.9%).

Weiagtige en ander nie-bloederige afskeidings het geen betekenis afgesien van dié van die verwante patologie nie.

'n Bloederige afskeiding uit die bors kan geassosieer wees met ander borspatologie, of kan slegs 'n aanduiding van abnormaliteit wees. Dit is met betrekking tot die behandeling van laasgenoemde groep dat daar sulke wyduiteenlopende menings bestaan.

In die 26 gevalle waaroor hier verslag gedoen word, was buispappiloom verreweg die mees algemene oorsaak. Verborge karsinoom is by 3 (11.5%) aangetref. In twee van hierdie gevalle was dit te wyte aan kwaadaardige ontaarding in 'n buispappiloom.

Die behandeling van tepelbloeding bestaan uit 'n ondersoek van die buis waaruit die bloed gepers word, en enige verdere stappe wat deur die bevindings aangedui word.

Mastektomie, as 'n primêre prosedure, moet nie onderneem word nie.

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DICUMAROL AS OORSAAK VAN ALOPECIA

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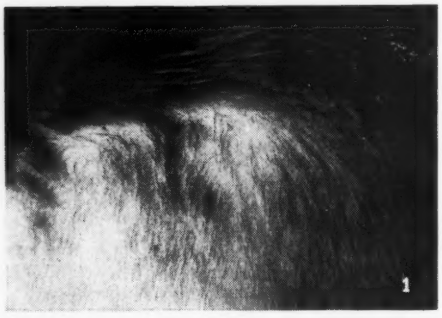
Die aandag is reeds dikwels op onaangename bywerkinge van anti-stollingsmiddels gevestig soos bv. eriteem, urticaria, maag-derm verskynsels, bloedinge, agranulositosis, ens. (vir literatuur sien Meyler[5]). 'n Minder bekende bywerking is haaruitval en sover bekend is hierdie verskynsel nognie in Suid-Afrika beskryf nie. Dit is merkwaardig, gesien die groot hoeveelhede van hierdie middels wat hier gebruik word.

Geval: 'n Blanke pasiënt van 48 jaar het in November 1958 'n aanval van koronêre trombose gehad. Hy is op 'n anti-stollings terapie, aanvanklik enkele dae op Heparin en daarna op Dicumarol, geplaas. Aangesien twee van sy broers reeds aan koronêre trombose oorlede is, is daar besluit om hom 'n voortdurende Dicumarol-behandeling te gee.

Voor sy siekbed het hy 'n welige haardos gehad. Hy was alleen met skilfers gepla. Ongeveer een maand na sy hartaanval het sy hare begin uitval tot ongeveer die helfte van wat dit tevore was. Die hare het ook van karakter verander deurdat hulle baie dunner geword het. Die haaruitval het geleidelik toegeneem totdat dit sedert ongeveer 'n maand voor die huidige ondersoek kaal kolle begin toon het.

By ondersoek word die volgende afwykings gevind:

Die hare op die kopvel is taamlik kort en op verskillende plekke is onreëlmatige kaal



kolle te sien (Fig. 1). Daar is 'n groei van fyn donshare tussen die oorblywende langer hare te sien. Dit is maklik in bossies uit te trek. Die hoofhuid vertoon 'n matige eksfoliasie. Wenkbroue, ooghare, oksel en pubis beharing vertoon geen afwykings nie. Aan die vingernaels kom 'n Beause lyn voor wat ooreenstem met die tyd van sy koronêre aanval. Verder vertoon die huid geen afwykings nie.

Bespreking: Cornbleet en Hoit[1] beskryf 'n geval van 'n tweejarige negerkind wat 'n diffuse alopecia ontwikkel het na die inname van rottegif. Die enigste ander vergiftigingsverskynsels was buikpyn, diarree en braking. By analise het dit geblyk dat die rottegif Warfarin (3-(a-pheniel b-asetiel)-4-hydroxycumarin) bevat het.

Daar was ook verlies van ooghare en wenkbroue. Die haaruitval het 17 dae na die vergiftiging begin en een maand later was die groei weer normaal.

Fisher (aangehaal deur Cornbleet en Hoit) beskryf hulle ondervinding met 100 gevalle waar deur verskillende anti-stolmiddels haaruitval veroorsaak is. (Liquemin, Thrombocid, Tromexan en Dicumarol). Die Heparin en Heparinoïde stowwe het in 50% alopecia veroorsaak. By die Cumarin groep was dit 42% en kombinasies van die twee groepe het tot 78% alopecia gegee. By twee gevalle was die alopecia blywend. Cornbleet en Hoit spreek hulle verbasing uit dat daar nie meer gevalle in Amerika beskryf word nie en hulle spekuleer oor moontlike redes hiervoor soos bv. die diffuse karakter van die haaruitval en die feit dat gesien die erns van die siekte daar gewoonlik nie veel aandag aan 'n bykomende alopecia bestee word nie.

Hirschboeck[4] beskryf gevalle van alopecia met 'n sinthetiese heperine (Natriumsout van gesulfureerde polygalacturine suur metiel ester metiel glucoside). Hulle het by 68 gevalle in 19% alopecia van die behaarde hoof, ooghare, wenkbroue, oksel en pubishare gevind. Merkwaardig is twee gevalle wat krulhare ontwikkel het terwyl hulle voorheen slank hare gehad het. In een geval was daar brosheid van vinger- en toonnaels. Die duur van die behandeling skyn geen invloed op die ontwikkeling van die alopecia te hê nie. Die insidensie was egter hoër by die gevalle wat 'n groter dosis van die middel gekry het. Die haaruitval het tot een maand na die begin behandeling eers begin.

* Dermatoloog.

Die patroon van haaruitval kom baie ooreen met die wat by thallium vergiftiging gesien word.

Geen verklaring is tot dusver vir hierdie verskynsel gegee nie. Interessant is die bevinding van Foldes wie vasgestel het dat 'n soutvrye dieet haaruitval verminder. Die vraag kan hier gestel word of soutretensie by hartpasiënte miskien 'n rol by die anti-stollingsmiddel alopecia speel.

Sover bekend is tot dusver geen gevalle gesien waar Phenindione preparate vir haaruitval verantwoordelik was nie.

Opsomming. 'n Geval word beskryf waar haaruitval na die toediening van Dicumarol ontstaan het.

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THE TREATMENT OF CORONARY ARTERY DISEASE

WITH PARENTERAL MAGNESIUM SULPHATE

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The current treatment of coronary artery disease must, we feel, be regarded as unsatisfactory. Most patients are treated with heparin or one of the modern oral anticoagulants but control is difficult and the treatment, while moderately successful, can give rise to dangerous side effects.

In this paper, we propose to discuss the treatment of coronary artery disease with magnesium sulphate which has not been used to any great extent except by Malkiel-Shapiro and Bersohn in South Africa.[1] A number of cases have been treated and clinical and biochemical investigations carried out before and after treatment. Biochemical investigations of coronary artery disease and atheroma as a whole must be based on a reasoned theory of the aetiology of these conditions.

Briefly, atheroma is a deposition of cholesterol on the endothelial lining of arteries. This is apt to occur where blood vessels undergo increased stress, i.e. the coronary arteries, the aorta, and where blood vessels, by their anatomical arrangement, branch at right angles to the aorta. Duguid[2] states that with increased blood flow, and consequent damage to the endothelial lining of an artery, mural thrombosis occurs. This can be seen particularly in the coronary and renal vessels, etc. which are subject to stress. The mural thrombi become organized and the endothelium tends to overgrow the clot, with a deposition of cholesterol. This in turn undergoes calcification with subsequent ulceration. Thus with the increased narrowing of the lumen of a blood vessel, especially the coronary vessels, decreased blood flow leads to the formation of a thrombus and complete occlusion.

Criticisms of Duguid's theory have been raised on the grounds that atheroma is no less common among haemophiliacs, but Copley[3] has deduced that mural thrombi are produced by the action of tissue and not blood thromboplastin.

A comprehensive literature has been compiled on the aetiology of atheroma, notably a recent review by Gilman.[4]

We feel that Duguid's theory is correct and that a state of affairs exists which physiologically can be reversed. This is borne out in the case of women in the child-bearing age when very little atheroma is observed. At the time of ovulation the total cholesterol content of the blood is somewhat reduced and an increase of fibrinolytic activity occurs, presumably due to the activation of plasminogen to

plasmin by the endometrium. Plasmin is a proteolytic enzyme and thus any mural thrombi present in the arterial tree may well be lysed.

Plasmin is a beta lipoprotein and is present in the blood as plasminogen, an inactive precursor. It is activated by certain substances such as streptokinase,[5] and naturally occurring activators present in brain, lung, uterus and tissue juices. It is of interest that chloroform is also an activator. However, a physiological balance is present and plasmin is markedly inhibited by certain substances. Some workers have suggested that the inhibiting agent is albumin, but our experiments suggest that this is, in fact, cholesterol. This is borne out by the fact that chloroform (chemically an inert substance whose sole action is the removal of cholesterol and other lipoids) can activate plasminogen to plasmin. Thus, with regard to women in the child-bearing age the fall of cholesterol may have, we feel, some bearing on the low inhibition of plasmin and its consequent increased activity. Furthermore, Greig[6] has demonstrated very high inhibition of plasmin following the ingestion of fatty meals.

Cholesterol appears to be loosely bound to the beta lipoproteins, but it would appear that the total cholesterol content is not so important as the ratio of this substance to lecithin, since lecithin, according to Deuel,[7] may:

1. Keep cholesterol in a colloidal state in plasma; and

2. May bind the lipoprotein and thus prevent the uptake of cholesterol.

Deuel's theory has been borne out by our investigations, which have demonstrated a decreased L:C ratio as suggested by Morrison[8] in cases of coronary artery disease and advanced atheroma. Electrophoresis has also shown a marked increase of the beta lipoproteins and a reduction in the alpha fraction, presumably due to the increased binding of the cholesterol to the beta proteins.

This brief summary may leave many gaps in our knowledge of the aetiology of atheroma and coronary artery disease and many problems remain to be solved. A point of interest is the incidence of coronary artery disease in sedentary workers (e.g. the bus driver *versus* the bus conductor), whilst a much lower figure is seen in those engaged in manual work. It is suggested that, on exercise, fibrinolytic activity is increased, according to MacFarlane,[9] and it is well known that increased metabolism is accompanied by a reduction of cholesterol.

Work carried out in South Africa by Bersohn and Oelofse[10] has shown that a significantly lowered serum magnesium level was found in Europeans when compared with the levels in the South African Bantu. They also had a much lower inhibition of plasmin[15] with much less incidence of coronary artery disease.

Further work by Malkiel-Shapiro and Bersohn[1] showed that by injecting 50% magnesium sulphate intramuscularly in cases suffering from acute myocardial infarction, marked beneficial results were obtained. In fact, 64 cases were treated with only 1 death.[16]

We have tried to produce a comprehensive biochemical investigation and clinical procedure. The biochemical tests carried out were:

1. Estimation of lecithin;
2. Estimation of total cholesterol;
3. Lecithin: cholesterol ratio;
4. Estimation of magnesium;
5. Fibrinolytic assay;
6. Electrophoresis of lipoproteins.

Complete clinical examination and electrocardiographic studies were performed on every patient before and after treatment, blood specimens being taken at a constant time, i.e. 1.30 p.m.

METHODS

Lecithin. King.[11]
Cholesterol. Zlatkis, Zake, and Boyle.[12] modified method of Rosenthal, Pfluke and Buscaglia.[13]
Lecithin: Cholesterol Ratio. Morrison.[8]
Serum Magnesium. Neil and Neely.[14]
Fibrinolytic Assay.

(A. PRINCIPLE):

It was decided to test for:
1. Spontaneous activity to detect any circulating plasmin;
2. Activated activity to estimate the amount of plasmin present; and
3. Inhibition to measure the degree of antagonism to this enzyme system.

METHOD

B. *Method*: Tube 1. (*Plasma Control*). 0.2 ml. of plasma, 4.8 ml. of Barbitone Buffer (pH 7.5).
Tube 2. (*Spontaneous Activity*). 0.2 ml. of plasma, 4.3 ml. of Barbitone Buffer, 0.5 ml. of Casein Substrate (2.5%).
Tube 3. (*Activated Activity*). 0.2 ml. of plasma, 4.2 ml. of Barbitone Buffer, 0.5 ml. of Casein Substrate and 100 units of Streptokinase (0.1 ml.).
Tube 4. (*Inhibition*). 0.2 ml. of plasma, 4.2 ml. of Barbitone Buffer, 0.5 ml. of Casein Substrate, 1 unit of Plasmin (bovine, 0.1 ml.).
Tube 5. (*Plasmin Control*). 4.4 ml. of Barbitone Buffer, 0.5 ml. of Casein Substrate, and 1 unit of Plasmin (bovine, 0.1 ml.).
All tubes were incubated for 1 hour in a water bath at 37° C. Deproteinization was carried out by the addition of 1 ml. of Trichloracetic Acid (20%). After centrifugalization, 4 ml. of the supernatant was removed and to this was added 6 ml. of Sodium Bicarbonate (12.5%) and 1 ml. of diluted Folin and Ciocalteu's reagent. The re-

leased tyrosine was compared in the EEL Absorptiometer and the units of fibrinolytic activity were computed from the control reading.

Casein was chosen as a substrate in order to avoid any contamination with plasmin which might occur following the use of fibrinogen and thrombin.

ELECTROPHORESIS

This was carried out using the Barbitone/Sodium Barbitone Buffer of Flynn, modified by the addition of an equal amount of 0.05 N. Sodium Caprylate. Whatman 3 mm. paper was used; 0.1 ml. of serum was applied: strips were stained for 18 hours with a saturated solution of Oil Red 0 in 60% Ethyl Alcohol and, after prolonged washing in running tap water, were scanned wet.

Results were assessed according to the following formula:

1. Below normal.
2. Low normal.
3. Mid normal.
4. High normal.
5. Above normal.

CLINICAL ASSESSMENT

This was carried out in the following basis:

A: Angina with positive ECG findings without myocardial infarction.

B: Proved myocardial infarction with positive ECG findings, with or without angina.

TREATMENT

Patients were given 1 c.c. of 50% Magnesium Sulphate intramuscularly every 5 days until 12 injections in all were given. However, we found that this was insufficient and the dose was increased to 2 c.c. Both biochemical and clinical investigations were carried out before and after treatment. In cases of acute myocardial infarction heparin was given in addition to magnesium sulphate for the initial 3 days of treatment. Heparin appears to lower the lipoid content of the blood quickly and also because of its anticoagulant effect, it was thought desirable to incorporate this drug.

RESULTS

The biochemical results (details of which are shown in the Appendix) do show some significant change after patients have been placed on magnesium therapy. Clinical results are, we feel, much more difficult to assess and time in most instances will be the factor of importance, although patients who have been treated along these lines have, in fact, greatly improved. Only one death has been seen in over 100 cases (at least one-third of which were acute myocardial infarctions) since this treatment was started. This was a case of heart block admitted too late for active treatment.

TABLE 1: ANALYSIS OF RESULTS AFTER MAGNESIUM THERAPY

	Reduced	*No Change*	*Increased*
Lecithin	34%	12%	54%
Cholesterol	82%	4%	14%
Lecithin : Cholesterol Ratios	0%	14%	86%
Magnesium	8%	0%	92%
Activation of plasmin	18%	38%	44%
Inhibition of plasmin	62%	34%	4%
Alpha lipoproteins ..	40%	28%	32%
Beta lipoproteins ..	66%	28%	6%

The results in this series are of special interest when compared with the admissions in the previous year when, of 196 cases admitted and treated with anti-coagulants but not with magnesium sulphate, 60 died.

Figs. 1–8 show the overall changes in the biochemical picture and the final analysis demonstrates the variations found in each case.

It will be appreciated that this work has been carried out solely to assess the biochemical and clinical changes following the injection of magnesium sulphate and to endeavour to probe its action. Hence there has been no attempt to carry out a series of controls (normal or otherwise), particularly in view of the severity of this disease.

The most outstanding changes are the reduction in cholesterol and the increase in magnesium sulphate levels, although this latter increase was obviously expected. While there is not the same degree of increase in the lecithin content, there is, however, a great improvement in the lecithin: cholesterol ratio which almost parallels the reduction in cholesterol. It would appear that this factor has far more significance than the lecithin or cholesterol levels alone and it will be seen that all patients, before treatment, had a lowered lecithin: cholesterol ratio as suggested by Morrison.[8] Lowering of the cholesterol level gives a consequent proportionate increase in lecithin and thus increases the latter's action in keeping cholesterol in a colloidal suspension, according to the theory of Deuel.[7]

There has been little change demonstrated in the activation of plasmin, but we feel this is not so important as the marked reduction in the inhibition. Our activation of this enzyme system by the use of streptokinase is not comparable with the action of tissue activators. Streptokinase works through a proactivator system and thus an additional factor is introduced. The reduction in inhibition confirms the work of Greig[6] and we feel that, with lowering of cholesterol, the inhibition of this enzyme system is decreased.

While the electrophoretic pattern shows no significant change in the alpha lipoprotein levels, there is a marked reduction in the beta content. We failed to find the constant pre-

sence of a pre-beta band and, in fact, in only a few cases was this phenomenon seen. It must be recorded that all these patients were diagnosed as myocardial infarction and we suggest that absence of a pre-beta band does not exclude this condition.

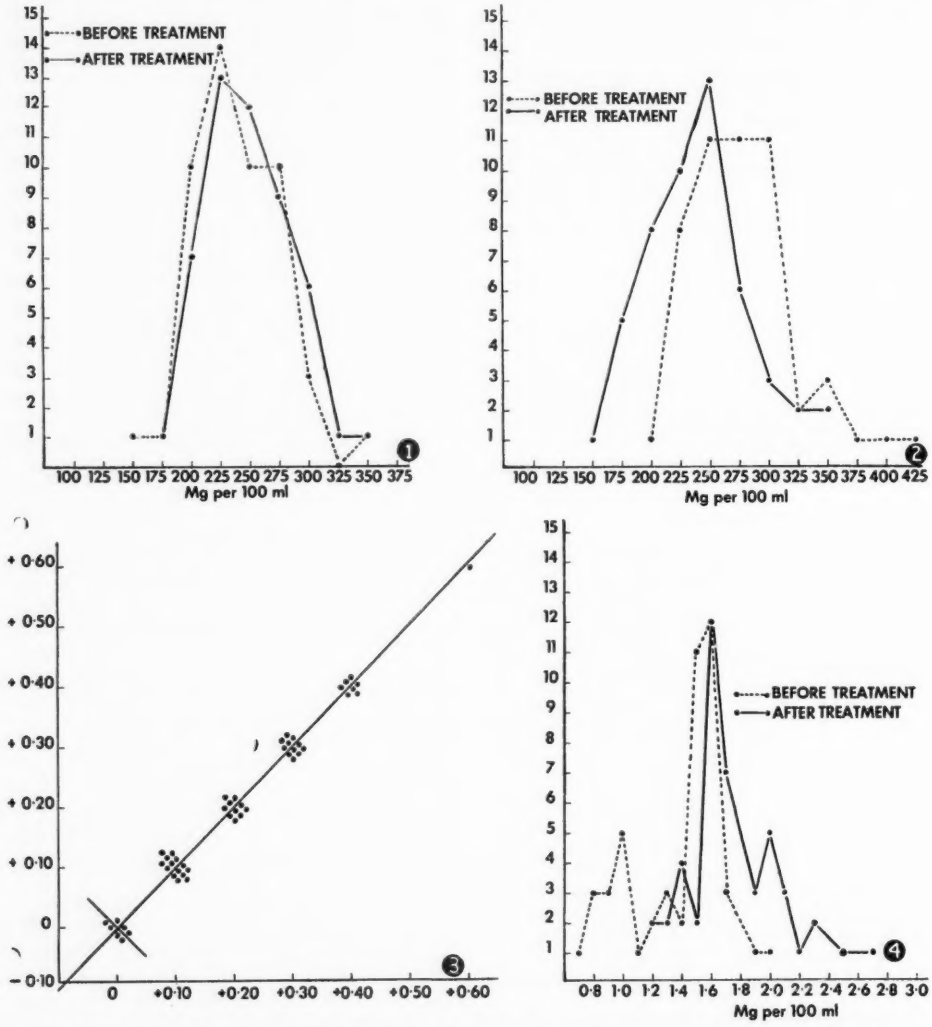


Fig. 1. Results of lecithin estimations before and after treatment with magnesium sulphate, demonstrating the lecithin level and the numbers of cases in which this was found, e.g. in 14 cases before treatment the lecithin estimation was 225 mg. per 100 ml. of serum. There is no apparent significant change following treatment.

Fig. 2. Cholesterol estimations before and after treatment, showing a significant decrease.

Fig. 3. The alteration in the lecithin cholesterol ratio after treatment. This ratio was obtained by dividing the lecithin in mg. per 100 ml. by the cholesterol in mg. per 100 ml.

Normal ratios should be above 1·0 and the results in this Figure were found by calculating the decimal alteration increase or decrease.

It will be noted that no decrease was evident and all cases showed either no change or a considerable increase.

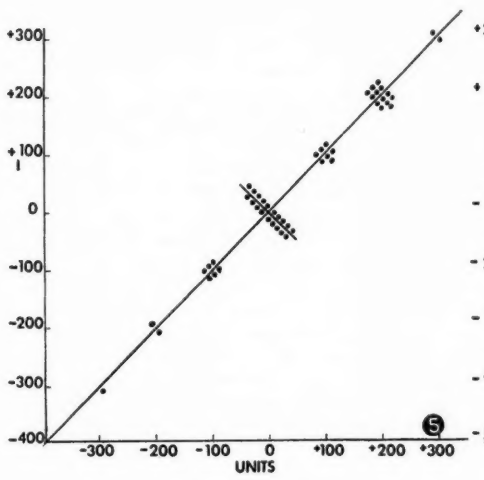
Fig. 4. Magnesium levels before and after treatment showing, as expected, a marked increase.

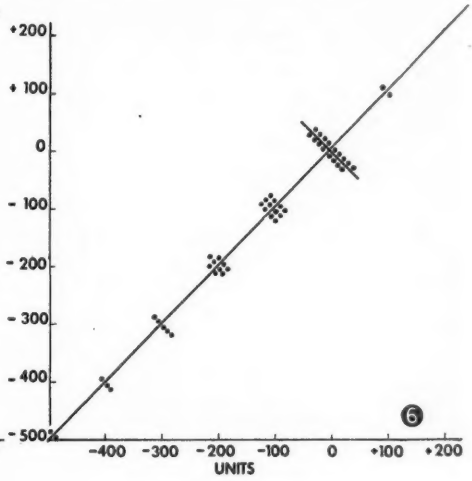
CASE REPORTS

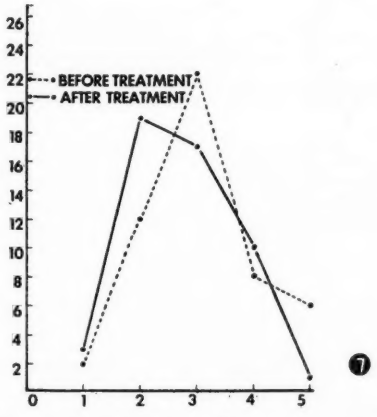
The following are typical case histories in each group:

Class A. Male (Age 47 years). In June 1955 he complained of substernal pain on exercise, following a severe cold 2 weeks before.

The heart sounds were normal, blood pressure 160/100 mm. Hg. and electrocardiographic recordings showed marked depression of the S-T intervals in leads 1, 2, V4, V5, and V6, greatly increased after exercise. He was thought to be suffering from toxic myocarditis. By 10 August 1955 his ECG tracings were normal, except for a sinus tachycardia.







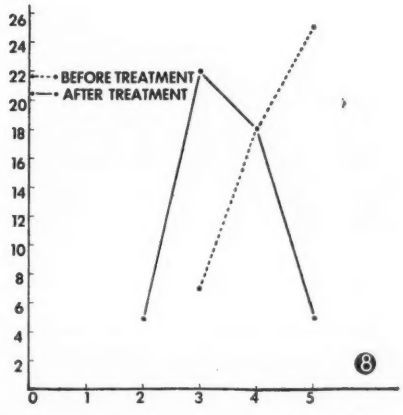


Fig. 5. The activation of plasmin, demonstrating the alteration in the number of units of fibrinolytic activity found after treatment.

While a considerable number of cases showed no change, there was a slight preponderance of cases showing some increase rather than a decrease.

Fig. 6. Demonstration of the reduction, in nearly all cases, of the degree of inhibition of plasmin after treatment.

Fig. 7. The alpha lipoprotein levels before and after treatment, showing no significant change.

Fig. 8. The beta lipoproteins levels before and after treatment, demonstrating a significant drop after treatment.

On 11 October 1955 he experienced a typical anginal pain on exercise and the abnormality in the ECG was a rather flat T wave in AVL. Since that date he has had typical angina. The diagnosis of myocarditis was reviewed and it was considered that this was a case of coronary insufficiency.

On 18 November 1957, substernal pain was present on effort and the ECG showed a somewhat depressed S-T interval in leads V4, V5, and V6, on exercise. Biochemical examination showed lecithin, 275 mg. per 100 ml.; cholesterol, 280 mg. per 100 ml.; L:C ratio 0.9; magnesium, 1.0 mg. per 100 ml.; spontaneous activity, 0 units %; activated activity, 260 units %; inhibition, 365 units %. He was given 1 c.c. of 50% magnesium sulphate every 5 days for 12 injections (intramuscularly).

The biochemical examination on 22 January 1958 showed: lecithin, 244 mg. per 100 ml.; cholesterol, 235 mg. per 100 ml.; L:C ratio, 1.0; magnesium, 1.7 mg. per 100 ml.; spontaneous activity, 0 units %; activated activity, 435 units %; inhibition, 150 units %.

On 13 June 1958, the angina was very much improved. No treatment given since January. He was recommended to continue magnesium sulphate injections every 2 weeks.

Class B (*Without Angina*). *Male* (*Age 50 years*). On 20 November 1955 he had a severe anterior wall infarction. He had a further attack on 14 February 1956, treated with heparin and Dindevan. He then led quite an active life doing his regular work and playing golf at weekends.

In November 1957 the ECG was still very abnormal. Biochemical examination showed: lecithin, 266 mg. per 100 ml.; cholesterol, 275 mg. per 100 ml.; L:C ratio, 0.9; magnesium, 1.0 mg. per 100 ml.; spontaneous activity, 0 units %; activated activity, 230 units %; inhibition, 500 units %.

He commenced magnesium sulphate injections 1 c.c. every 5 days, but on the fifth injection he had a severe posterior wall infarction.

Biochemical examination then showed: lecithin, 220 mg. per 100 ml.; cholesterol, 230 mg. per 100 ml.; L:C ratio, 0.9; magnesium, 1.6 mg. per 100 ml.; spontaneous activity, 0 units %; activated activity, 390 units %; inhibition, 300 units %.

The dose of magnesium sulphate was increased to 2 c.c. every other day and he made an uninterrupted recovery after he had completed his 12 injections.

Biochemical investigations showed: lecithin, 200 mg. per 100 ml.; cholesterol, 150 mg. per 100 ml.; L:C ratio, 1.3; magnesium, 1.6 mg. per 100 ml.; spontaneous activity, 0 units %; activated activity, 450 units %; inhibition, 100 units %. He is now on a maintenance dose of 2 c.c. of 50% magnesium sulphate fortnightly.

On 17 May 1958 his biochemical examination was: lecithin, 280 mg. per 100 ml.; cholesterol, 245 mg. per 100 ml.; L:C ratio, 1.1; magnesium, 2.5 mg. per 100 ml.; spontaneous activity, 0 units %; activated activity, 450 units %; inhibition, 300 units %. He is doing full work and playing golf.

It is noted that he developed his last attack after the fifth injection of magnesium sulphate and it is questionable if the dose of 1 c.c. was sufficient to prevent an attack.

Class B (*With Angina*). *Married Woman* (*Age 67 years*). On December 1953 she had a myocardial infarction but it was not severe. Electrocardiographic tracings showed inverted and 'coronary' T waves in V4 and Ve. This was followed by angina of effort and continued to 15 October 1957, when she had several severe attacks and her electrocardiographic recordings showed inverted and 'coronary' T waves in leads 3, V1, V2, V3 and V4. Her angina was definitely more severe.

Her biochemical investigations on 15 October 1957 showed: lecithin 232 mg. per 100 ml.; cholesterol, 300 mg. per 100 ml.; L:C ratio, 0.7; magnesium, 1.4 mg. per 100 ml.; spontaneous activity, 0 units %; activated activity, 660 units %; inhibition, 500 units %. She was placed on 1 c.c. of 50% magnesium sulphate intramuscularly every 5 days for 12 injections. Her angina was very much improved.

On 2 January 1958 her biochemical investigations showed: lecithin, 275 mg. per 100 ml.; cholesterol, 225 mg per 100 ml.; L:C ratio, 1.2; magnesium, 1.7 mg. per 100 ml.; spontaneous activity, 0 units %; activated activity, 390 units %; inhibition, 40 units %.

She was given no more magnesium sulphate until 2 April 1958. Her biochemical picture deteriorated and the L:C ratio dropped to 0.9. Since then she has had a maintenance dose of 2 c.c. of 50% magnesium sulphate fortnightly and her L:C ratio has improved to 1.0. Her angina is steadily improving.

In nearly all cases of angina there has been a definite improvement. One case has remained the same. However, the majority of healed myocardial infarctions had no symptoms but whether further attacks have been prevented it is difficult to say.

DISCUSSION

It is evident that the work of Malkiel-Shapiro and Bersohn has been confirmed. The mode of action of magnesium remains obscure, but the following hypotheses are suggested:

1. Since magnesium is a protein-bound ion, it may compete with cholesterol for attachment to the beta proteins and do so successfully since cholesterol is bound only loosely to the beta protein molecule, whilst magnesium is a much more positive ion and thus the released cholesterol can then be metabolized and excreted in the faeces.

2. Magnesium may act as a catalyst with the lipases in the metabolism of fat.

We feel that the former hypothesis is more correct but further work is necessary to test this theory. We suggest the utilization of radioactive magnesium and the detection of its presence in the beta proteins.

It is of interest that the feeding of magnesium sulphate by mouth in a limited number of cases has produced no significant change in the biochemical or clinical picture.

Once again it would appear that cholesterol is the essential factor in the production of atheroma and allied conditions.

Various queries present themselves:

(*a*) Can atherosclerotic arteries be returned to normal?

(*b*) Can the disease be halted before thrombosis occurs?

(*c*) Of what value is a diet low in fat?

(*d*) Is increased exercise necessary?

Here we must quote the autopsy findings in cases of chronic alcoholism, advanced cases of starvation and cachexia. It is well known that such cases are virtually devoid of atheromatous lesions but, obviously these must have been present at some time. Could it be that a poor and insufficient diet has been responsible for the absence of such lesions at the time of death?

To-day, and especially among the professional classes, very little exercise is taken and day-to-day living consists mainly of sitting in surgeries or offices. Walking is almost unknown, travel by car, bus or train being the rule. To revert to the analogy of the bus driver and bus conductor, the former sits down most of the day and obtains little exercise, while the latter spends the day on his feet with constant exercise. Whilst the driver is prone to myocardial infarction, the conductor is not.

It may be that the modern way of living, with little exercise and large meals, is conducive to the recent marked increase of coronary disease, which must have been less prevalent in the slower tempo of our forefathers' days, although we have no doubt that their diet was much more abundant than ours.

We feel that a certain degree of exercise is essential in order to get rid of our excess calories and we know that the consequent increased metabolism decreases the cholesterol content of the blood, leading to the whole chain of beneficial biochemical effects.

We suggest that the modern concept of the after-treatment of myocardial infarction needs a radical overhaul and that patients should not be treated as chronic invalids and 'mollycoddled,' but should be encouraged to take a reasonable amount of exercise and live a full life.

Magnesium sulphate therapy is not the complete answer, but is a step in the right direction and is a simple treatment which can be safely given by the practitioner without the necessity for constant and elaborate laboratory control.

In cases of acute myocardial infarction, the use of heparin in small doses in addition to the magnesium sulphate is advised for the initial 3 days—not for its anticoagulant value but for its lipoid-clearing properties.

The effects of magnesium therapy do not appear to be permanent and a maintenance dose of 2 c.c. given fortnightly for 6 months appears to be necessary. The patient's condition should be reassessed at the end of this period.

The advantages of administering magnesium orally are obvious and it is proposed to carry out further investigations using different salts of magnesium.

SUMMARY

1. Over 100 patients suffering from coronary heart disease (of which at least one third were acute myocardial infarctions) were treated with intramuscular magnesium sulphate with only one death, while 196 cases of acute myocardial infarction treated with routine anticoagulants gave a 30% mortality.

2. Biochemical investigations were carried out before and after treatment in 50 cases.

3. An analysis of the biochemical and clinical changes is given.

4. The possible action of magnesium sulphate is discussed and also possible effects of diet and exercise.

5. Suggestions are put forward for the treatment of myocardial infarction by the practitioner in the patients' own home.

We wish to thank Messrs. Parke, Davis of Detroit, U.S.A. and Lederle Laboratories of New York, U.S.A., for kindly supplying bovine fibrinolysin and streptokinase respectively.

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APPENDIX

BIOCHEMICAL RESULTS BEFORE AND AFTER TREATMENT WITH MAGNESIUM SULPHATE

Case	*Group*		*Lecithin*	*Cholesterol*	*L/C Ratio*	*Mg.*
1.	A	Before	200	230	0·8	2·1
		After	250	205	1·2	2·7
2.	A	Before	200	210	0·9	1·7
		After	242	260	0·9	2·1
3.	B	Before	255	305	0·8	1·5
		After	300	325	0·9	1·7
4.	B	Before	230	240	0·9	1·5
		After	222	235	0·9	2·0
5.	B	Before	270	270	1·0	1·6
		After	250	220	1·0	1·8
6.	A	Before	220	235	0·9	1·5
		After	293	280	1·0	2·2
7.	A	Before	205	220	0·9	1·6
		After	333	325	1·0	2·2
8.	B	Before	240	250	0·9	0·7
		After	275	205	1·3	1·9
9.	B	Before	220	250	0·8	1·5
		After	236	255	0·9	1·4
10.	B	Before	200	280	0·7	1·25
		After	233	210	1·1	1·9
11.	B	Before	225	300	0·7	1·5
		After	226	210	1·0	1·8
12.	A	Before	275	290	0·9	1·2
		After	230	220	1·0	1·6
13.	B	Before	155	230	0·7	1·5
		After	266	200	1·3	1·9
14.	A	Before	257	290	0·9	1·8
		After	275	270	1·0	1·9
15.	B	Before	216	260	0·8	1·5
		After	260	250	1·0	1·7

BIOCHEMICAL RESULTS BEFORE AND AFTER TREATMENT WITH MAGNESIUM SULPHATE

Case	*Group*		*Lecithin*	*Cholesterol*	*L/C Ratio*	*Mg.*
16.	B	Before	262	305	0·8	1·2
		After	222	200	1·1	1·9
17.	A	Before	240	250	0·9	1·5
		After	238	225	1·0	1·6
18.	B	Before	271	300	0·9	1·0
		After	270	250	1·0	1·8
19.	A	Before	200	270	0·7	0·8
		After	260	260	1·0	1·6
20.	A	Before	275	280	0·9	1·0
		After	255	244	1·0	1·7
21.	B	Before	355	380	0·9	1·6
		After	300	305	0·9	2·0
22.	B	Before	200	260	0·8	1·1
		After	220	250	0·9	2·1
23.	A	Before	230	260	0·8	1·1
		After	266	200	1·2	1·4
24.	B	Before	230	350	0·6	1·5
		After	230	230	1·0	1·6
25.	B	Before	240	250	0·9	1·0
		After	200	165	1·2	1·9
26.	B	Before	178	240	0·7	1·0
		After	350	350	1·0	1·8
27.	A	Before	238	280	0·8	0·9
		After	266	220	1·2	1·6
28.	A	Before	302	405	0·7	1·6
		After	275	280	0·9	1·3
29.	B	Before	275	330	0·8	0·9
		After	275	275	1·0	1·9
30.	A	Before	200	225	0·9	1·6
		After	225	180	1·2	1·7
31.	A	Before	260	275	0·9	1·5
		After	200	170	1·1	1·6
32.	A	Before	255	260	0·9	1·6
		After	210	200	1·0	1·7
33.	B	Before	230	305	0·7	1·6
		After	220	220	1·0	1·8
34.	B	Before	250	275	0·9	1·3
		After	270	260	1·0	1·6
35.	B	Before	253	350	0·7	1·3
		After	273	280	0·9	1·4
36.	B	Before	284	415	0·7	0·8
		After	311	310	1·0	1·6
37.	B	Before	266	275	0·9	1·0
		After	200	180	1·3	1·6
38.	A	Before	275	290	0·9	1·4
		After	257	220	1·1	1·9

BIOCHEMICAL RESULTS BEFORE AND AFTER TREATMENT WITH MAGNESIUM SULPHATE

Case	*Group*		*Lecithin*	*Cholesterol*	*L/C Ratio*	*Mg.*
39.	B	Before	232	300	0·7	1·4
		After	275	225	1·1	1·7
40.	B	Before	266	360	0·7	1·6
		After	230	255	0·9	1·6
41.	B	Before	209	250	0·8	1·6
		After	250	250	1·0	1·6
42.	B	Before	256	302	0·8	1·0
		After	275	260	1·0	1·5
43.	A	Before	230	220	1·0	2·0
		After	230	170	1·3	1·9
44.	B	Before	300	330	0·8	0·8
		After	257	350	0·7	1·2
45.	A	Before	216	225	0·9	1·7
		After	183	150	1·1	1·8
46.	B	Before	280	305	0·9	1·6
		After	310	290	1·0	1·8
47.	B	Before	266	305	0·8	1·6
		After	272	250	1·0	2·5
48.	B	Before	305	315	0·9	1·6
		After	234	265	0·9	1·6
49.	A	Before	235	250	0·9	1·6
		After	305	300	1·0	1·7
50.	B	Before	230	270	0·8	1·5
		After	253	240	1·0	1·8

			Fibrinolytic Assay			*Electrophoresis**	
Case	*Group*		*Spontaneous Activity*	*Activated Activity*	*Inhibition*	*Alpha*	*Beta*
1.	A	Before	0	390	290	3	5
		After	0	360	240	3	3
2.	A	Before	0	350	350	2	3
		After	0	380	320	4	5
3.	B	Before	0	290	225	2	4
		After	0	365	205	3	4
4.	B	Before	0	395	225	5	4
		After	0	340	250	5	5
5.	B	Before	0	490	230	2	3
		After	0	420	200	3	2
6.	A	Before	0	500	300	1	5
		After	0	495	290	2	2
7.	A	Before	0	350	270	5	5
		After	0	385	260	3	4
8.	B	Before	0	230	330	3	5
		After	0	405	180	2	4

* 1. Below normal. 2. Low normal. 3. Mid-normal. 4. High normal. 5. Above normal.

Case	Group		Fibrinolytic Assay			Electrophoresis*	
			Spontaneous Activity	Activated Activity	Inhibition	Alpha	Beta
9.	B	Before	0	350	290	3	5
		After	0	430	260	2	3
10.	B	Before	0	365	550	5	5
		After	0	470	200	2	3
11.	B	Before	0	165	250	2	5
		After	0	305	220	3	5
12.	A	Before	0	365	250	4	4
		After	0	330	100	4	4
13.	B	Before	0	365	330	3	5
		After	0	385	135	2	3
14.	A	Before	0	803	660	3	4
		After	0	445	150	3	4
15.	B	Before	0	250	250	3	4
		After	0	425	180	3	3
16.	B	Before	0	500	330	2	5
		After	0	235	110	3	3
17.	A	Before	0	330	250	5	5
		After	0	315	75	1	3
18.	B	Before	0	250	200	3	5
		After	0	370	150	4	5
19.	A	Before	0	365	330	4	5
		After	0	500	95	2	3
20.	A	Before	0	260	365	3	4
		After	0	455	150	4	5
21.	B	Before	0	315	250	2	5
		After	0	500	200	4	4
22.	B	Before	0	430	210	2	3
		After	0	360	185	2	3
23.	A	Before	0	460	500	2	4
		After	0	340	110	1	3
24.	B	Before	0	340	275	5	4
		After	0	510	50	4	4
25.	B	Before	0	340	180	2	4
		After	0	330	180	3	3
26.	B	Before	0	350	150	3	4
		After	0	365	152	2	2
27.	A	Before	0	160	600	3	5
		After	0	350	130	2	3
28.	A	Before	0	325	290	4	5
		After	0	440	200	4	4
29.	B	Before	0	350	300	3	4
		After	0	375	180	3	2
30.	A	Before	0	390	250	2	5
		After	0	450	155	2	3

* 1. Below normal. 2. Low normal. 3. Mid-normal. 4. High normal. 5. Above normal.

Case	Group		Fibrinolytic Assay			Electrophoresis*	
			Spontaneous Activity	Activated Activity	Inhibition	Alpha	Beta
31.	A	Before	0	230	330	2	4
		After	0	520	55	3	4
32.	A	Before	0	530	230	3	4
		After	0	402	250	2	4
33.	B	Before	0	300	250	3	5
		After	0	560	50	3	4
34.	B	Before	0	330	200	4	5
		After	0	260	135	2	3
35.	B	Before	0	566	633	4	5
		After	0	315	180	4	4
36.	B	Before	0	165	365	4	5
		After	0	420	300	2	3
37.	B	Before	0	230	500	3	4
		After	0	330	205	2	3
38.	A	Before	0	390	280	3	4
		After	0	390	205	4	4
39.	B	Before	0	660	500	4	5
		After	0	390	40	3	4
40.	B	Before	0	300	305	3	5
		After	0	500	80	3	4
41.	B	Before	0	330	190	1	5
		After	0	350	200	2	3
42.	B	Before	0	200	260	4	4
		After	0	520	60	4	4
43.	A	Before	0	340	135	3	3
		After	0	530	55	3	3
44.	B	Before	0	480	250	3	3
		After	0	365	135	4	4
45.	A	Before	0	270	200	3	4
		After	0	300	200	2	3
46.	B	Before	0	480	350	3	3
		After	0	500	220	3	3
47.	B	Before	0	390	200	3	5
		After	0	400	200	2	4
48.	B	Before	0	400	450	3	4
		After	0	360	300	1	3
49.	A	Before	0	500	230	2	3
		After	0	310	290	3	3
50.	B	Before	0	310	260	4	5
		After	0	320	210	2	2

* 1. Below normal.
2. Low normal.
3. Mid-normal.
4. High normal.
5. Above normal.

ON EQUIPPING A HEART-LUNG UNIT

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The past decade has been a period of stimulation and progress for the cardio-vascular surgeon. The pioneers of the forties, Churchill, Gross, Craaford, Blalock, Brock, Bailey and Harken, had proved that direct heart surgery was safe and successful. Open heart surgery with the aid of hypothermia became an accomplished fact, though, because of time restriction, only simple lesions were operable. Gibbon and Clark had spent many years attempting to develop machines which could take over the functions of the heart and lungs to allow for more extensive intra-cardiac operations. However, it was not the surgeon alone who solved the problems, for almost every branch of medicine was somewhere concerned in a vital manner. In 1953 Gibbon's work was crowned by the first human open heart operation using a pump-oxygenator.[4] Lillehei and Kirklin (the former utilizing the bubble oxygenator described by deWall and the latter the surface oxygenator of Gibbon) have shown that the technique can be used safely for many diverse heart lesions. Surgeons in South Africa have not been backward in the experimental and clinical application of the method.[1, 6, 7] There are now 3 separate units where open heart surgery is practised and in at least 3 others experimental work is far advanced and the clinical use of the heart-lung pump is imminent. Our own clinical experience was preceded by a 3-year experimental programme in which over 200 dogs were operated upon. During this time we realized the importance of collaboration between medical and non-medical personnel skilled in mechanical and electronic techniques.

The organization of a heart-lung team is a matter of some complexity, and the expense of adequate equipment is great. As a unit develops there is a continuous need for modifications and improvements and for new apparatus not previously catered for. This paper describes the various instruments we have developed and which, after thorough experimentation before use on humans, have been found equal to the demands made upon them. This report may be of help to others engaged in similar work and is intended to draw the attention of the medical profession to the considerable technical potential this country possesses for manufacturing complicated electronic and mechanical equipment.

HEART-LUNG PUMP

A heart-lung unit consists essentially of 2 independent parts, the pumps and the oxygenator. Many types of pump embracing different principles have been developed. Ideally a pump should simulate the heart's action so that it is capable of a pulsatile output in accordance with the patient's needs and in a manner producing negligible destructive effects upon the components of the blood. No such pump has as yet been produced. After considerable experience with the Sigmamotor type of pump we decided to use a de Bakey type of pump head.

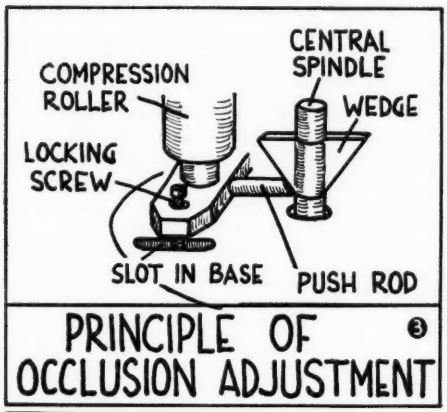
Three types of oxygenator have been described—the surface oxygenator, the bubble oxygenator and the membrane oxygenator—and many modifications of each have been designed. There is no conclusive proof as to which is the safest and most efficient and, to us, it seems that the essential need is for a team to decide upon the method and then to use it on animals until its potentialities and limitations are fully understood. We have adopted the bubble oxygenator described by deWall. The oxygenator can be used with any type of pump just as the pumps are adaptable to any form of oxygenator.

The Pump. Our present machine contains 3 pump units. These, together with 2 electro-thermometers, 2 oxygen flow-meters and a thermostat unit, are assembled on a cabinet (18 inches high, 24 inches wide, and 36 inches

⅜ inch diameter each revolution of the pump ejects 20 c.c. of blood; hence the maximum output of the venous and arterial pumps with this tubing is 6,000 c.c. per minute and that of the cardiotomy pump 3,000 c.c. per minute. Using ½ inch tubing the output is increased by more than 50%.

The venous and cardiotomy pumps have associated speed meters calibrated in revolutions per minute. The indication has been obtained by the simple expedient of measuring the voltage fed to the motor, the speed being a linear function of this voltage from 15–300 r.p.m. This method is inaccurate when the pump operates against resistance and a more reliable arrangement which operates whether the pump is driven manually or by the motor is used for the arterial pump. A small generator is geared to the pump drive shaft and the current it develops registers on a meter calibrated in revolutions per minute. This system is independent of the voltage fed to the motor and therefore gives an accurate reading irrespective of the speed or strain of the pumps.

The 2 electronic telethermometers are used to register the temperature of the patient and the water-bath. A thermistor element, incorporated in a probe, is connected by cable to a Wheatstone bridge. Changes of temperature alter the thermistor resistance which unbalances the bridge and this gives a meter reading which is a reflection of temperature. Controls are included for calibration and the initial setting of the potential applied to the bridge.



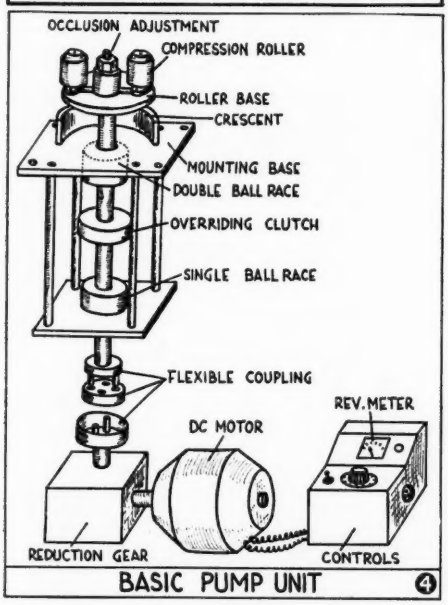


Fig. 3. Diagram showing the method used for adjusting the position of the compression rollers so as to attain fine occlusion of the tubing passing through the pump. (*See text.*)

Fig. 4. Diagram of general assembly of a pump unit.

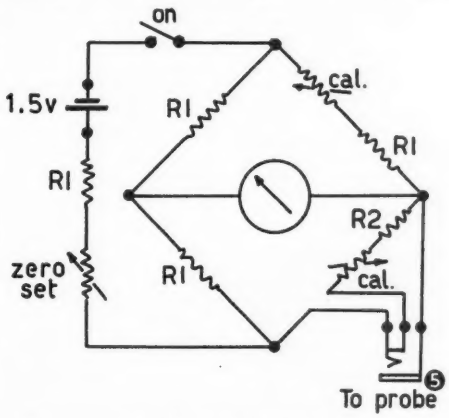


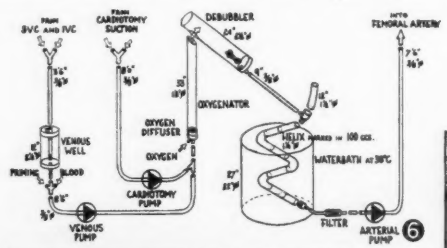
Fig. 5. Circuit diagram of electronic thermometer.

A circuit diagram is shown in Fig. 5. The current is derived from a dry cell torch battery which is easily changed. A separate electrothermometer constructed on the same principle is available for continuous post-operative temperature recordings.

Two oxygen flow-meters are used, one for each oxygenator of the deWall system. They are mounted to the right of the control panel adjacent to where the oxygenator is placed. They are of the Système Gauthier and work in any position. They register flows within the range of 0–15 litres per minute.

The pump cabinet also contains a thermostat relay into which the sensing element, set for 38°C., is plugged. In addition there is an energy regulator of the Simmerstat type with a pilot light, and this provides control of the water-bath temperature in the event of thermostat failure.

The Oxygenator. We have used the bubble oxygenator described by deWall. The apparatus and circuit differs slightly from that of deWall and of Phillips and Barnard[7] because the roller type of pump does not require a Latex rubber pump segment and Tygon tubing is brought directly through the pump. We have dispensed with a cardiotomy well and introduce the cardiotomy blood directly into the circuit immediately before entering the oxygenator. These modifications reduce connexions, length of tubing and priming volume. All connectors are made locally of highly polished stainless steel. Two complete sets are available, one for a 3/8 inch circuit for flow rates below 3,500 c.c. per minute and one of ½ inch for higher flow rates. They are polished to a finish of approximately 20 microns, a standard comparable with that of imported connexions. Neoprene Seal-O-rings are used as washers between the Nylon oxygen diffuser and the mixer stopper and, since adopting these, blood and oxygen leaks have not been troublesome. Mayon tubing is used for the cardiotomy well, the mixing chamber, the debubbling chamber and the helix, otherwise Tygon tubing of 3/8 or ½-inch bore is utilized. For emergency use spare sterile tubing of all dimensions is stored in sealed Polyvinyl bags. The oxygenator circuit for low flow perfusions is shown in Fig. 6. For flow rates of over 2,000 c.c. per minute double oxygenators and debubblers are used. The water-bath is placed on a low trolley mounted on 4-inch castors. The oxygenators and debubblers are held by clamps fixed to an adjustable upright support. The whole oxygenator is placed immediately to the right of the pumps and, being low-mounted, enables the operator to see and reach any part of the circuit from his position in front of the pump unit (Fig. 7).



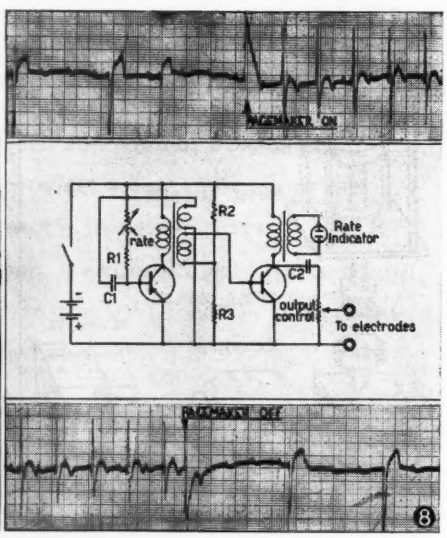


Fig. 6. Diagram showing details of circuit and connections of the DeWall oxygenator. The circuit shown here is that used by our unit and is modified slightly from DeWall's original description.

Fig. 7. Photograph showing completed assembly of pump and oxygenator under actual theatre conditions.

Fig. 8. Circuit diagram of portable pace-maker. Mounted above and below the circuit are electrocardiographic tracings showing the effectiveness of the pace-maker in producing an adequate beat. Heart block had been produced in a dog by injecting Novocaine into the ventricular septum of the exposed heart.

Transistorized Pacemaker. During the repair of ventricular septal defects there is a danger of injury to the conducting bundle of His and the production of heart block. The use of Isoprenaline Sulphate[5] has reduced the mortality of this complication, but the danger remains high. The outlook is further improved by a pacemaker which stimulates the heart to contract at a rate capable of maintaining an adequate circulation. External stimulation, by placing the electrodes on the chest wall,[8] can maintain an adequate heart beat, but when there is a need for prolonged control, skin burns occur and the contractions of adjacent muscles become unbearably painful. Lillehei advises that the electrodes be sewn into the myocardium. We find experimentally that sewing the electrodes into the pericardium gives satisfactory heart stimulation without skeletal muscle contraction, though the method has only been used in acute experiments.

A portable pacemaker which operates from two 2.5 volt mercury cells has been built. The total current consumption of the unit is 7 milliamps. Two controls are included, one to vary the output pulse rate from 50 to 120 per minute and the other to control the strength of the stimulus. In designing a unit for direct stimulation of the heart, the output pulse should have a sharp rise time and be of short duration. The effectiveness of a stimulus depends on its duration and its voltage and, by increasing the one, the other can be reduced. However, it has been shown that impulses of short duration are more efficient, and the pacemaker described gives a peak pulse of 15 volts with a pulse duration of 10 milliseconds. The circuit is shown in Fig. 7. The effectiveness of the unit is illustrated in Fig. 8.

This pacemaker is intended primarily for use during transportation of the patient from theatre to ward after operation and also for the patient with heart-block who would otherwise be well enough to be ambulant. It is said that the patient can learn to increase the rate of stimulation according to the needs of the moment and this can readily be done with our unit. It is designed to fit into a pocket and contains sufficient power to last for many hours of continuous use. Adequate warning of impending exhaustion of power is provided by the need to increase the strength stimulus to produce an adequate beat. The mercury cells can be replaced rapidly. A second larger unit is available which can operate from the mains as well as from a dry battery source. This unit can be connected to an ECG machine which monitors the heart beat and can be adjusted so that if the heart ceases to beat for a variable length of time (up to 2 seconds), the pacemaker will automatically switch on and stimulate the heart at a pre-set rate and strength.

Defibrillator. No theatre should be without a cardiac defibrillator, for many lives can be saved by having this instrument available at every major operation. Our experience on experimental animals, confirmed by observation on humans, is that provided the fibrillating heart is adequately oxygenated, an appropriate shock will restore co-ordinated rhythm. Under the conditions of an open heart operation using a heart-lung pump it is always possible to oxygenate the heart fully by perfusing the heart with oxygenated blood. Ventricular fibrillation under these conditions becomes a matter of little concern provided an effective defibrillator is on hand. On one occasion when an aortic aneurysm had been excised under deep hypothermia (the temperature had been reduced to 12° C.) the heart fibrillated during re-warming when the temperature was 17° C. Warming continued without attempts at electrical defibrillation until the body temperature had reached 33° C., a period of 45 minutes during which the heart was continuously perfused with arterialized blood. A single shock of 120 volts of 0.2 seconds duration restored normal rhythm. This had been a recurring experience with experimental animals, ventricular fibrillation being the rule during the re-warming phase of profound hypothermia experiments. Defibrillation has always been accomplished with one or two shocks.

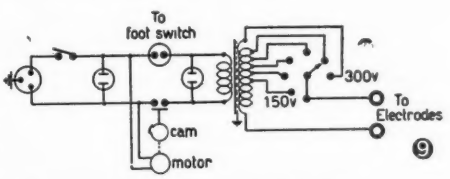


Fig. 9. Circuit diagram of the defibrillator.

The unit provides a large alternating current of 1 amp. at selected voltages between 100 and 300 of approximately 0.2 second duration. The general circuit arrangements are shown in Fig. 9. This unit could be considerably elaborated by the inclusion of adjustable pulse duration controls, but it has proved reliable in its present form with a fixed pulse duration output. The machine is mounted in a leather casing and is portable.

DISCUSSION

The various instruments described have passed the experimental stage and are available for human use. We have now done 12 human open heart operations and have had no deaths which could be attributed to the pump-oxygenator or to failure of the instruments described. The pumps have been used together with disposable plastic oxygenators for 4 cases of nitrogen mustard perfusion of malignancies involving the legs, one involving the arm and one the pelvis. These low flow perfusions have all been accomplished without incident.

Several other pieces of equipment are only being used experimentally. Heat-exchange units for direct blood cooling and warming have been used in one human operation, the temperature being dropped to 12° C., and in a number of dog experiments. Once the temperature drops to below 25° C. it is necessary to continue the cooling with the aid of pumps to by-pass the heart.[3] The object of these experiments is to lower the temperature until the heart stops spontaneously and the circulation can be totally arrested for a considerable period of time without damage to vital organs. Under such conditions prolonged aortic or intracardiac surgery could be accomplished.

A small portable 2-pump unit has been constructed. This is intended to be used for hypothermia and nitrogen mustard perfusions of regions where at operation an irremovable malignancy has been found. With portable pumps, sterilized tubing contained in cellophane bags and a disposable oxygenator, it is possible to assemble the equipment whilst the surgeon exposes the regional vessels for cannulation.

This article has been written to indicate the potentialities we possess in South Africa of undertaking work requiring complex electronic equipment but the clinical efficacy of which is not definitely proved. For instance, it is not yet known whether nitrogen mustard perfusion of regional malignancies is of much clinical value; neither is it known whether profound hypothermia is a technique which can be used with safety on humans. In the state of chronic poverty in which our hospitals exist it is not possible to expend considerable amounts of money on the purchase of equipment which might never be used on humans. We have so often had to wait until methods were clinically proven overseas before applying them here. Local industries can supply precision equipment cheaply and rapidly and their engineers can modify and improve the units as the need arises. This has enabled us to embark upon work of a highly experimental nature without being submerged by the twin bogies of cost and delay. Our experience encourages us to continue with our policy of local development of electronic and mechanical appliances. The engineers concerned visit our experimental laboratory and see the problems we face from week to week. They are able to correct, to modify or to improve on their machines, and in the end something of real value may result.

Even though the acquisition of equipment has been facilitated by the co-operation of the firms of Middleton and Anderson, and Benington and Son, of Johannesburg, nothing would have been accomplished without the financial assistance of the C.S.I.R. of South Africa, the Nuffield Foundation and the Council of the University of the Witwatersrand. We wish to thank Mr. L. Fatti for his assistance and guidance, Drs. V. Wilson and E. Joubert for help and suggestions. Mr. D. Adler allowed us to study the roller mechanism of his imported pump from which we derived considerable practical help for which we are grateful. We are deeply indebted to the Cape Town Unit, particularly to Drs. C. Barnard and M. MacKenzie, for the facilities and assistance which they always generously accord to us.

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4. Gibbon, J. H. (1954): Minn. Med., **37,** 171.
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NOTES AND NEWS : BERIGTE

A MEDICAL TOUR OF EUROPE

Another medical tour of Europe (now in its third year) for a group of South African doctors and their wives will take place from 26 April to 3 June 1960.

The medical programme, arranged by Mr. P. B. Mayer, Medical Bookseller, of P.O. Box 713, Cape Town, will include visits to Clinics, Universities, Hospitals and various specialized medical and pharmaceutical centres in Austria, Switzerland and England to suit the special interests of the individual members.

There will also be a varied programme of sightseeing which will include visits to Rome, Vienna, Basel, Zurich, Lugano, Grindelwald, Berne, Geneva, Paris, Amsterdam, London, Cambridge, etc.

Members may extend their stay in Europe for additional postgraduate work or touring upon completion of the general programme.

Dr. Louis F. Freed, M.A. (S.A.), D.Phil. (Pret.), D.Phil. (U.O.V.S.), M.D., D.P.M. (Rand.), F.R.S.S.Af., of Johannesburg, was recently appointed a member of a Board of Examiners in the Department of Psychology of the University of South Africa.

Dr. Freed recently established a post-graduate prize in the Department of Psychiatry of the University of Witwatersrand. The prize will be awarded annually to a post-graduate student who distinguishes himself in the examination for the Diploma in Psychological Medicine.

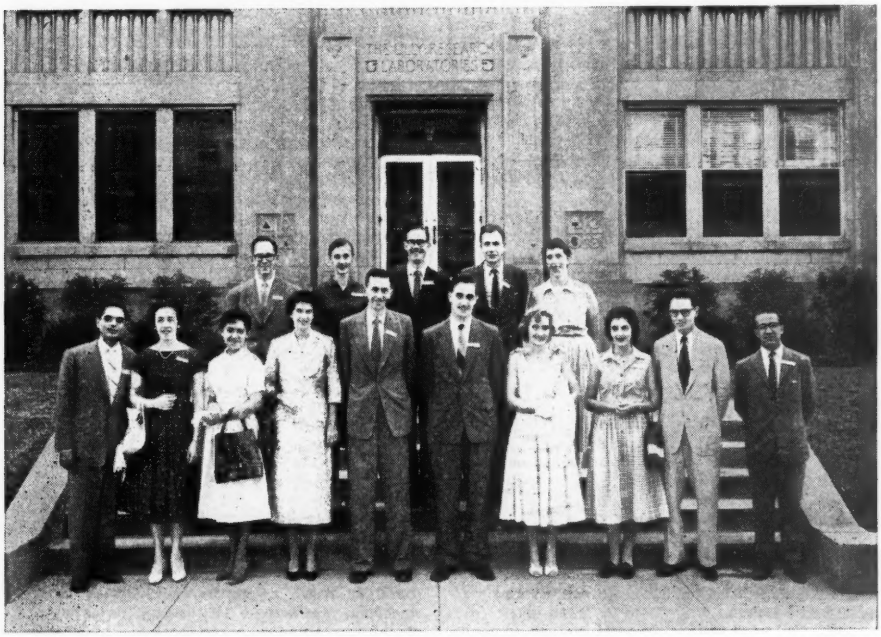
* * *

ELI LILLY MEDICAL RESEARCH FELLOWS

Nine physicians from Latin America, Australia, England, Scotland, and Union of South Africa were guests of Eli Lilly and Company, Indianapolis, from 1–4 September 1959. All of the Lilly guests have been active in medical teaching institutions or in private practice in their native countries and are engaged in postgraduate medical studies in the United States under Lilly postgraduate educational fellowships.

The Lilly Educational Fellowship Program, which sponsors physicians from all areas of the free world who wish to come to the United States to further their medical studies, was established shortly after World War II. The aim of the fellowship program is to promote a better understanding and to establish closer ties between members of the medical profession in the United States and other countries, and to contribute to postgraduate medical education. Physicians selected to participate in the fellowship program are chosen by fellow members of the medical profession in their home countries. While in the United States, they study in medical colleges or institutions of their own selection. Their studies may be in general medicine and its related fields or any of the medical specialties. One hundred and ten fellowships have been granted to physicians from other countries under the fellowship program since 1945.

Each year before their return to their native countries, the Lilly Fellows and their wives visit the Lilly research and manufacturing facilities in Indianapolis. The tour of Lilly operations includes a visit to the research facilities and a firsthand inspection of the research projects being carried out by the company. A visit is also made to the Lilly Laboratory for Clinical Research at the Marion County General Hospital, as well as a tour through the manufacturing facilities at the McCarty Street and Kentucky Avenue plants and the Biological Laboratories at nearby Greenfield, Indiana. An interesting side light of the trip is a visit to the famous Indianapolis automobile race track, home of the 500-Mile speed and endurance classic which is held once each year on May 30.



Top Row: (*Left to Right*) Dr. Lazaro Isaac Gidekel (*Argentina*). Mrs. Edwards, Dr. Kenneth David Gilmore Edwards (*Australia*), Dr. Cedric William Malcolm Wilson (*Scotland*), Mrs. Wilson. *Bottom Row*: (*Left to Right*) Dr. Rafael Oswaldo Rodriguez (*Venezuela*), Mrs. Rodriguez, Dr. Leticia Perez Suarez (*Mexico*), Mrs. Dowdle, Dr. Eugene Bernard Davey Dowdle (*South Africa*), Dr. John D. Griffiths (*England*), Mrs. Griffiths, Mrs. Azevedo, Dr. Decio Faraco de Azevedo (*Brazil*), Dr. Luis A. Alexander (Bolivia).

BOOTS MEDICAL APPOINTMENTS DIARY FOR 1960

The Boots diaries have now arrived in South Africa. Medical practitioners wishing to obtain a copy of this useful desk diary should write immediately to:

B.P.D. (S.A.) (Pty.) Ltd.,
P.O. Box 45,
Jeppestown, Transvaal.

* * *

Mr. H. E. Lewy, Cape Representative for Medical Distributors (Pty.) Ltd., has moved into new premises at 20 Barrack Street, Cape Town.

The showrooms and offices are on the ground floor of President House, facing Corporation Street and just around the corner of Plein Street.

The 'Dismed' range covers a large variety of surgical instruments, medical appliances, electromedical apparatus and hospital equipment which should be of interest to medical practitioners and hospital administrators alike.

Mr. Lewy extends a cordial invitation to old and new friends to call in at 20 Barrack Street at their convenience.

The telephone number (41-1172) and Post Office Box 195, Cape Town, remain unchanged.

Mnr. H. E. Lewy, Kaapse Verteenwoordiger van Medical Distributors (Edms.) Bpk., het verskuif na 'n nuwe perseel te Barrackstraat 20, Kaapstad.

Die vertoonkamers en kantore is op die grondverdieping van President House, teenoor Corporationstraat en net om die hoek van Pleinstraat.

Die 'Dismed' reeks dek 'n groot verskeidenheid chirurgiese instrumente, mediese toebehore, elektromediese apparate en hospitaal uitrusting wat van belang behoort te wees vir beide mediese praktisyns en hospitaal-administrateurs.

Mnr. Lewy nooi ou en nuwe vriende vriendelik uit om hom 'n besoek te bring te enige tyd by Barrackstraat 20.

Die Telefoonnommer (41-1172) en Posbus 195, Kaapstad, bly onveranderd.

PREPARATIONS AND APPLIANCES

VALLERGAN 10 MG. TABLETS

Maybaker (S.A.) (Pty.) Ltd. announce that 10 mg. tablets of *Vallergan* brand trimeprazine tartrate are available now in a packing of 500 tablets in addition to the packing of 50 tablets.

Vallergan is supplied, in addition, as a syrup containing 4 fluid oz. in each bottle. This presentation is indicated for the relief of pruritus in various dermatological conditions such as atopic dermatitis, neurodermatitis, chronic urticaria and infantile eczema.

It is also supplied as *Vallergan Forte* syrup for oral pre-anaesthetic medication of children, especially those of 30 to 50 lb. body-weight.

DEQUALONE-P

Allen & Hanburys (Africa) Limited announce the introduction of a cream containing the potent antimicrobial agent, Dequadin (Dequalinium) in combination with prednisolone. The preparation provides antibacterial, antifungal, anti-inflammatory, anti-pruritic and anti-allergic properties in the management of skin diseases.

Indications: Dequalone-P is indicated in the treatment of any acute or chronic skin disease with an inflammatory, allergic or infective basis. In the treatment of pruritic dermatoses, the presence of Dequadin is particularly valuable in preventing secondary infection in virtue of its wide antibacterial and antifungal spectra of activity. Dequadin is effective against strains of staphylococci resistant to penicillin and to other antibiotics and its use diminishes the risk of development of resistant strains. Dequalone-P is rapidly effective in the management of contact dermatitis, neurodermatitis, seborrhoeic dermatitis and intertrigo. Eczemas of various types, including allergic eczema, infantile eczema and varicose eczema respond often within seven days. Recurrences of most forms of eczema are common and when they occur a further course of Dequalone-P should be given. In the presence of infection over a wide area, it is often advantageous to control the infection with Dequadin cream before commencing the use of Dequalone-P.

Contra-Indications: Dequalone-P should not be used in the treatment of burns or of herpes simplex.

Application: Dequalone-P is non-greasy and does not stain either skin or clothing. Before application of Dequalone-P, the skin should be cleansed, preferably without soap, and the cream applied sparingly, with or without a dressing. It should not be vigorously rubbed into the skin. The hydrophilic nature of the base ensures rapid penetration.

Presentation: Dequalone-P is supplied in tubes each containing 5 grammes of cream.

DEQUADIN PESSARIES

Allen & Hadburys (Africa) Limited announce the introduction of a product which provides a new treatment for vaginitis. Each pessary contains 10 mg. Dequadin (Dequalinium) chloride, a substance which has earned high clinical repute in virtue of its wide antibacterial and antifungal properties.

Indications. Dequadin pessaries are indicated for the treatment of vaginitis caused by monilial infection, trichomonal infection or by infection with mixed bacterial and fungal species. Treatments of monilial and non-specific bacterial vaginitides are accompanied by high rates of complete eradication of infection and rapid relief of symptoms is observed in almost all cases. In trichomonal vaginitis, complete clearance of infection is obtained with more difficulty, but cure, as demonstrated by disappearance of *Trichomonas vaginalis* from the vaginal discharge, may be expected in 40–60% of cases after treatment over a period of six weeks. A notable feature of published observations on the treatment of trichomonal vaginitis with Dequadin pessaries has been the relief of often intolerable irritation and discomfort after treatment for between 24 and 72 hours. So often in cases of trichomonal vaginitis a mixed infection is present and there is no doubt that, in such cases, there is considerable merit in using a preparation with the wide antimicrobial spectrum of Dequadin. As opposed to the antibiotics, the acquisition of bacterial resistance to Dequadin is unknown.

Dosage: One pessary should be inserted, as high in the vagina as possible, night and morning. An applicator designed to provide a simple means of inserting the pessaries is supplied with each pack. Douching, either before or after insertion of a pessary, is unnecessary. If douching is considered to

be desirable in severe cases, a soap solution should not be used. During pregnancy it may be desirable to insert the pessaries without the applicator. It is recommended that treatment be continued for three weeks in cases of monilial or bacterial vaginitis and for a period of up to six weeks in trichomonal vaginitis. Even if symptoms rapidly disappear, a treatment of this duration may be required to eliminate infection.

Presentation: Dequadin pessaries, containing Dequadin chloride in a non-irritating, non-staining, non-greasy and rapidly dispersible base, are supplied in boxes containing 30 pessaries, sealed in metal foil. A special applicator is supplied with each pack.

PREDSOL NASAL DROPS

PREDNISOLONE PHOSPHATE FOR TREATMENT OF HAY FEVER AND OTHER ALLERGIC CONDITIONS

Description: Predsol Nasal Drops contain 0.1% prednisolone disodium phosphate in isotonic buffered solution. This compound, being soluble, achieves thorough contact with the inflamed tissues, thus producing maximum therapeutic effect.

Indications: Hay fever; vasomotor and non-seasonal allergic rhinitis.

Treatment: *Hay fever*: When symptoms develop, apply two drops to each nostril four times a day. The nose usually becomes normal in one to three days but full dosage should be continued for three or four days more, then tailed off over another two to three days. Any recurrence of symptoms will usually respond to a further one day's treatment.

Vasomotor and non-seasonal allergic rhinitis: Apply two drops in each nostril four times a day. Continue for a few days after good symptomatic response is obtained; then reduce dosage to minimum satisfactory maintenance level.

Freedom from side-effects: The daily amount of prednisolone used, being under 1 mg., is too small to give rise to systemic effects.

Contra-indications: Septic conditions of the nose demanding specific chemotherapy.

If primary rhinitis has become secondarily infected, the infection should be treated before using Predsol Nasal Drops.

Storage: Protect from light and store in a cool place.

Pack: Predsol Nasal Drops 10 cc. bottle with dropper.

Glaxo Laboratories (S.A.) (Pty.) Ltd., Manchester Road, Wadeville, Transvaal.

PREDSOL SKIN PREPARATIONS

PREDNISOLONE PHOSPHATE WITH OR WITHOUT NEOMYCIN FOR DERMATOLOGICAL USE

Description: *Predsol Skin Ointment* No. 1 (non-greasy): 0.5% prednisolone disodium phosphate in water-miscible base.

Predsol-N Skin Ointment No. 1 (non-greasy): 0.5% prednisolone disodium phosphate with 0.5% neomycin sulphate in water-miscible base.

Predsol Skin Lotion: 0.25% prednisolone disodium phosphate in a transparent aqueous liquid.

All are colourless, non-irritating and do not stain the skin.

Advantages: Prednisolone phosphate is soluble and thus secures more thorough contact with inflamed tissues, so obtaining better therapeutic effect.

When infection is present or suspected, concurrent antibiotic therapy is available in Predsol-N Skin Ointments.

Predsol Skin Lotion spreads evenly and thinly and is practically invisible when applied, although it does not completely dry off.

Indications: Anal and vulvar pruritus; Contact dermatitis of various types; Allergic eczema, food eczema, infantile eczema; Eczematoid reactions of the eyes and ears; Neurodermatitis; Nummular dermatitis; Seborrhoeic dermatitis.

Application: *Ointments*: A small quantity is applied to the affected area two or three times a day.

Lotion: A small amount is spread evenly on the area two or three times daily.

Storage: Store in cool place.

Packs: Predsol Skin Ointments No. 1: 5 gram tube.

Predsol-N Skin Ointments No. 1: 5 gram tube.

Predsol Skin Lotion: 20 cc. plastic "squeeze" bottles.

Glaxo Laboratories (S.A.) (Pty.) Ltd., Manchester Road, Wadeville, Transvaal.

PREDSOL-N NASAL SPRAY

PREDNISOLONE PHOSPHATE, WITH NEOMYCIN, FOR RELIEVING CONGESTIVE INFLAMMATORY CONDITIONS

Composition:

Prednisolone disodium phosphate	0.025%
Neomycin sulphate	0.5%
Naphazoline nitrate	0.025%

In aqueous solution.

Advantages: Prednisolone phosphate, being soluble, achieves thorough contact with the inflamed tissues, and thus provides the most efficient local therapy.

Naphazoline nitrate, a decongestant vasoconstrictor, allows the prednisolone to exert its maximum effect; the low concentration present minimises any risk of the "rebound phenomenon."

The antibiotic, neomycin, helps to control any associated infection.

Indications: Various commonly occurring inflammatory allergic conditions of the nose.

Administration: With nozzle inserted in nostril, quickly and firmly squeeze the bottle, whilst inhaling. Three sprays into each nostril are usual for an adult; for children one or two sprays are usually sufficient.

The preparation may also be used as drops by inverting the bottle and squeezing gently. One to two drops into each nostril every three hours should be sufficient for children, or two to three drops for adults.

The length of treatment varies with the condition and the response obtained. Unnecessarily prolonged treatment should be discouraged.

Storage: Protect from light and store in a cool place.

Pack: 15 cc. plastic spray bottle.

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PREDSOL EYE AND EAR PREPARATIONS

PREDNISOLONE PHOSPHATE, WITH OR WITHOUT NEOMYCIN, FOR INFLAMMATORY CONDITIONS

Description: *Predsol Drops for Eye or Ear*: 0.5% prednisolone disodium phosphate in sterile isotonic buffered solution.

Predsol-N Drops for Eye or Ear: 0.5% prednisolone disodium phosphate with 0.5% neomycin sulphate in sterile isotonic buffered solution.

Predsol Eye Ointment: 0.5% prednisolone disodium phosphate in a bland paraffin base.

Predsol-N Eye Ointment: 0.5% prednisolone disodium phosphate with 0.5% neomycin sulphate in a bland paraffin base.

Advantages: Being soluble, prednisolone phosphate is readily accessible to the inflamed tissues, thus producing maximum therapeutic effect.

When infection is present or suspected, concurrent antibiotic therapy is available in Predsol-N Drops and Eye Ointment.

Predsol Eye Drops, having the prednisolone in solution, avoid any risk of irritation due to particulate matter.

Indications: *Eye Conditions*: Inflammation caused by trauma, infection or other irritants. Treatment is most beneficial in acute and self-limiting conditions. Local treatment is fully effective when only the anterior segment of the eye is affected; involvement of deeper tissues may require systemic therapy.

Ear Conditions: Inflammatory conditions, such as otitis externa, due to infection or other causes.

In both eye and ear conditions Predsol-N preparations should be used when infection is present or suspected.

Application: *Drops for Eye or Ear*: One or two drops instilled in eye every one or two hours (perhaps with use of ointment at bedtime).

Two or three drops instilled into the ear every two or three hours until control is achieved, when frequency can be reduced.

Eye Ointment: Apply every three or four hours.

Storage: Store in cool place. The Drops should be protected from light.

Packs: Predsol Drops for Eye or Ear: 3 cc. vial with dropper.

Predsol-N Drops for Eye or Ear: 3 cc. vial with dropper.

Predsol Eye Ointment: 3 gm. tube with ophthalmic nozzle.

Predsol-N Eye Ointment: 3 gm. tube with ophthalmic nozzle.

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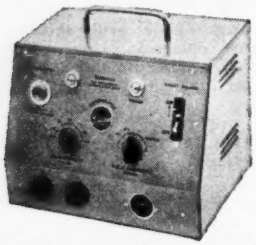
CARDIAC RESUSCITATION INSTRUMENTS

Cardiac resuscitation apparatus is being recognized as part of the standard emergency equipment for every operating theatre. This was the opinion expressed by many anaesthetists and surgeons attending the 42nd Medical Congress at East London.



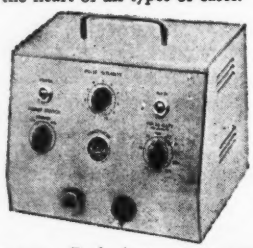
A Cardiac *Defibrillator* which has all the essential features required in such equipment plus a number of desirable special features is manufactured by the Birtcher Corporation and distributed in South Africa by Medical Distributors (Pty.) Ltd. of Johannesburg and Cape Town.

The exclusive features of the Birtcher *Defibrillator* are:

1. A built-in circuit breaker. Should the electrodes accidentally touch each other, the circuit breaker will automatically cut out and there is no delay in looking for a replacement fuse, or opening the unit to insert it. All one has to do is to return the switch on the control panel of the apparatus to the 'on' position.

2. The electrodes are concave in shape to mould themselves evenly to the contours of the ventricles. The rubber insulation of electrode holders and cords is of a heavy quality and may be autoclaved.

3. The impulses administered to the patient may be varied in intensity from 0-160 volts and a duration of 0.1, 0.5 or 1 second may be selected or the apparatus may be manually operated. Both these variable factors are of importance so that the correct impulse and intensity can be produced to defibrillate the heart of all types of cases.

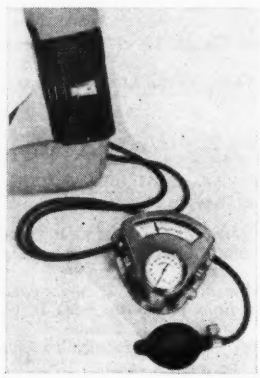


As a companion set Medical Distributors offer the Birtcher *Heartpacer* which may be used for internal or external pace-making. The 2 units are readily identified by their distinctive colouring—*Red* for the *Defibrillator* and *Green* for the *Heartpacer*. Both instruments are approved by Underwriters Laboratories, which is a guarantee for utmost safety to patient and Theatre Staff.

Further particulars from: Medical Distributors (Pty.) Ltd., P.O. Box 3378, Johannesburg or P.O Box 195, Cape Town.

THE OSCILLOTEST FOR MEASURING THE BLOOD PRESSURE

The Oscillotest is designed in accordance with the *Pachon* system. The apparatus is cleverly contrived for easy operation and exact determination of the systolic and diastolic blood pressures. The setting-in and decrease of the pulse beat can be read off exactly. The advantage of this method lies in the elimination of personal errors.



Further uses: determining the blood circulation possibly still present in drowned persons and babies, investigation of heart activity during anaesthesia and blood transfusion, in organic injuries necessitating amputation, in partial paralyses and nervous injuries, in cardiac dilatations, etc.

Further information concerning the genuine 'Friedrich Bosch Oscillotest' may be obtained from the sole South African Agents: Zenith Medical and Surgical Instruments (Pty.) Ltd., Medical Arts Building, 220 Jeppe Street, P.O. Box 4367, Telephone 22-2069, Johannesburg.

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